L 10,5
A 102

ACTA PÆDIATRICA

REDACTORES:

IN DANIA: C. E. BLOCH, KÖBENHAVN, S. MONRAD, KÖBENHAVN. IN FENNIA: ELIS LÖVEGREN, HELSINGFORS, ARVO YLPPÖ, HELSINGFORS. IN HOLLANDIA: E. GORTER, LEIDEN, J. HAVERSCHMIDT, UTRECHT, CORNELIA DE LANGE, AMSTERDAM. IN NORVEGIA: TH. FRÖLICH, KRISTIANIA, AXEL JOHANNESSEN, KRISTIANIA, CARL LOOFT, BERGEN. IN SUECIA: I. JUNDELL, STOCKHOLM, A. LICHTENSTEIN, STOCKHOLM, WILH. WERNSTEDT, STOCKHOLM.

EDITOR: I. JUNDELL, STOCKHOLM

Vol. III. Supplementum

17: V. 1924

Almqvist & Wiksells Boktryckeri-Aktiebolag
UPPSALA 1924

ACTA PÆDIATRICA

EDITOR PROFESSOR I. JUNDELL

8 ARTILLERIGATAN, STOCKHOLM

The 'ACTA PÆDIATRICA' contain articles relating to pediatrics. These articles are published in English, French or German, according to the wishes of the author. Each number consists of about 6 printed sheets, 4 numbers forming a volume. The numbers will be issued as soon as the articles sent in can be printed. The 'Acta' is open to articles from foreign authors in all countries, if sufficient space can be found for them. Manuscripts are to be sent direct to the Editor, to whom also enquiries about the exchanging of papers are to be directed. The subscription should be forwarded to the Editor. Each volume costs 20 Swedish crowns or 25 shillings or 5 dollars.

ACTA PÆDIATRICA enthalten Arbeiten aus dem Gebiete der Kinderheilkunde. Die Arbeiten werden, je nach eigener Wahl des Verfassers, in deutscher, französischer oder englischer Sprache veröffentlicht. Jedes Heft enthält cirka 6 Druckbogen; 4 Hefte bilden einen Band. Die Hefte erscheinen, je nachdem die in dieselben aufzunehmenden Aufsätze druckfertig vorliegen. Die Acta nehmen nach Möglichkeit auch Arbeiten ausländischer Verfasser aller Nationen auf. Manuskripte nimmt der Herausgeber entgegen, desgleichen Wünsche betreffs Austausch von Zeitschriften. Abonnementanmeldung bei dem Herausgeber. Preis pro Band 20 schwedische Kronen.

Les ACTA PÆDIATRICA contiennent des ouvrages du domaine de la pédiatrie. Les études sont publiées en français, anglais ou allemand au choix de l'auteur. Chaque fascicule contient env. 6 feuilles in -8°; 4 fascicules forment un volume. Les fascicules paraissent au fur et à mesure que les articles y destinés sont imprimés. Les Acta reproduisent, dans la mesure du possible, les articles d'auteurs étrangers de tous les pays. Les manuscrits doivent être expédiés à l'éditeur, à qui les demandes relativement à l'échange de journaux devront également être adressées. Abonnement chez l'éditeur. Prix par volume Cr. Suéd. 20 ou 40 Fr. francs.

ACTA PÆDIATRICA

UNIVERSITY OF MICHIGAN LIBRARIES

STUDIES IN SCURVY

BY

J. AXEL HÖJER

Former First Assistant at the Children's Clinic
of the Karolinska Institutet, Stockholm.
(Chief: Professor I. Jundell.)

This work has been carried out by aid of grants from the Karolinska Institutet and the Swedish Society for Medical Research.

UPPSALA 1924

ALMQVIST & WIKSELLS BOKTRYCKERI-A.-B.

Medical
Smith + Zeit
11-4-49
WB793

To

Professors Axel Holst and Theodor Frölich

This work is respectfully inscribed by

THE AUTHOR

CONTENTS

Preface 7
Introductory 8
Methods of experimental scurvy, from Holst to the latest investigators 9

Part I.

Examination of the antiscorbutic value of some vegetable products.

Survey of experiments 18
Summary; discussion; conclusions 22

Part II.

Histo-pathological studies.

Preliminary notes.
Introductory 29
The macroscopic changes 30
Technique 31
Nomenclature 32
Classification of scurvy in different stages 33
Grouping of the material within these stages 36
Chapter I. The bone formation in scurvy.
Teeth 38
The endosmal ossification 48
The enchondral ossification. Cartilage 50
*
Four cases of infantile scurvy 60
*
Summary and conclusions of Chapter I. 64
Chapter II. Muscles.
The skeleton musculature 68
Heart 79
Chapter III. Liver 82
Chapter IV. Spleen 91
Chapter V. Kidney 96
Chapter VI. Adrenal 100
Chapter VII. Salivary glands 104
Chapter VIII. Lung 107
Chapter IX. Blood and vessels. Hemorrhages in scurvy 109
Chapter X. Connective tissue 114

Part III.

Discussion of some scurvy problems.

Chapter I. Scurvy and infection 115
Chapter II. Disposition 122
Chapter III. Latent scurvy 123
Chapter IV. The calcium metabolism in scurvy 126
Chapter V. Scurvy and rickets 128
Chapter VI. Inanition and scurvy 129
Chapter VII. A modified method for experimental rating of the antiscorbutic value of a product 130
Chapter VIII. Pathogenesis of scurvy. Relation of scurvy to other deficiency diseases 132

Summary and conclusions of Parts II and III 139

Part IV.

Scurvy and tuberculosis.

Chapter I. Historical 140
Chapter II. Experimental study on guinea-pig.
Technique and survey of experiments 148
Influence of scurvy on tuberculosis 154
Influence of tuberculosis on scurvy 162
Chapter III. Experimental study on man.
Survey of experiment 164
Criticism and conclusion 169

Summary and conclusions of Part IV 170

Part V.

Records of cases.

Cases belonging to Part I 172
» » » » II, Chapter I 200
» » » » IV, » II 206
» » » » IV, » III 234

Literature cited: 265
List of authors 275

94 microphotograms.
33 curves in the text.
6 colured plates.

Preface.

The work which is here presented was begun in July, 1922. It would have been impracticable to fulfil it without the possibilities of technical aid offered by clinical laboratories. To Professors F. Henschen and G. Häggquist, who have allowed me to avail myself of these possibilities and to whom I am also indebted for much helpful advice, I beg to express my gratitude. My thanks are also due to Professors I. Jundell and U. Quensel, to Assistant Professor Dr. C. Kling, Doctors R. Nordgren, G. Vestbeck, H. Davide, A. Wassén, S. Sive, A. Wallgren, Å. Åkerlund, the Dental Surgeon Dr. G. Westin, and others, for various reasons, some of which I have mentioned more particularly in my book. Special thanks are due to Doctor F. Wahlgren and Fil. Doctor L. G. Romell who have kindly read the proofs.

My late father, the historian Nils J. Höjer, who during all his life, beside his practical activity as a teacher, devoted himself to scientific work for science's sake, has been my model. My wife, Signe Höjer, has been my helper.

I have allowed myself as a respectful token of admiration to inscribe my work to Professors Axel Holst and Theodor Frölich in Christiania, the first investigators in the field of experimental scurvy, whose work still remains unrivalled. Even though the exaggeration is evident in Funk's utterance (1922): »Since the experiments of Holst and Frölich, no real progress has been made (in experimental scurvy), in spite of the numerous publications that have appeared», yet his words show how high Holst and Frölich's works rank among all the rest.

Hagalund, Sweden. February 1924.

J. Axel Höjer.

Introductory.

After the strenous research during the last twenty years of a number of distinguished investigators, it has now been proved that scurvy has to be looked upon as *one* disease in adults, young children and infants, in monkeys and guinea-pigs, with the same etiology, the same unknown pathogenesis, similar clinical symptoms and patho-anatomical changes, and identical therapeutics (MacCallum). Scurvy, however, is above all a diesease of growth, and the most profitable studies have been made in quickly growing organisms, human infants or young monkeys and guinea-pigs. As surely as the quicker growth is a fundamental physiological factor, which principally distinguishes the undeveloped organism of the child from the developed organism of the adult and constitutes pediatrics as a special branch of medical science, as surely the scurvy problem is a central pediatric problem.

The plan which from the first I had drawn up for this work was the following. I wished 1) in connection with the study of the antiscorbutic substance of some Swedish wild berries[1] to examine the scorbutic changes which might be expected in liver, muscles and teeth, and to take up some scurvy problems for discussion; and 2) to study the mutual relations of scurvy and tuberculosis. As the result began to show clearer, I have widened the plan, and especially I have extended the patho-anatomical studies as far as the material available after the *post-mortem* examinations has allowed, in order by this means to support the new conception of the pathogenesis of scurvy, which presents itself as the final result of these studies. Many organs are left out, and among those lacking are the thyroid glands, the sexual organs, the hypophysis. Before long, I am going to publish complementary investigations, which have been carried on, but are not as yet brought into definitive form.

[1] With »strawberries» are in the following always meant wild wood-strawberries, *Fragaria vesca* L., and not *Fragaria moscata*.

Methods of experimental scurvy from Holst to the latest investigators.

In 1907, A. Holst showed that a diet of cereal and water induces scurvy in young guinea-pigs, and together with T. Frölich he then submitted different scurvy problems to a resultful examination, using guinea-pigs for the experiments. Their results having been confirmed from many quarters, the antiscorbutic substance (or group of substances) was ranged as vitamin C (Drummond in 1919) among the vitamins (Funk), or the accessory food factors (Hopkins). Still the guinea-pig is the animal most frequently used for scurvy experiments. It is only the introduction of the monkey (Hart and Lessing 1913) that has been a good addition, but through its quicker growth, easiness to handle, and cheapness, the guinea-pig has considerable advantages as experimental animal.

Holst and Frölich's basal diet, different kinds of cereal and water, is absolutely free from antiscorbutic factor. All the later investigators have confirmed the statement that the progress of scurvy in guinea-pigs on such a diet is very uniform. The nature and sequence of the symptoms may be studied in the works of Holst and Frölich (1907, 1912), Cohen and Mendel (1918), Hess (1920). I give a short extract of their descriptions. After a symptom-less period of one or two weeks after the animals have been put on absolute diet, the first pathological sign appears, signalling the onset of the disorder. This first sign may vary, sometimes it is a loss of weight, sometimes a tenderness of joint or an inordinate excitability of the animal, which soon changes into inertness. After two or three weeks the animals show an unwillingness to move which has been ascribed to the swollen, tender joints, around which there are numerous hemorrhages, also in the musculature. Often they try to protect some specially affected joint by continually holding the corresponding limb lifted, »the scurvy position» of Chick, Hume and Skelton. The teeth become loosened and the incisors frequently break off. The coat is rough. Very often fractures occur at the

epiphyseal lines of the long tubular or medullated bones. The hemorrhagic diathesis may be extended to all tissues and after three, four or five weeks the animal succumbs, after having lost about a third of its weight at the beginning of the experiment. The results found at the *post-mortem* examination may be summarized thus: 1) Hemorrhages, most numerous and largest in and about the epiphyseal ends of the long bones; 2) Atrophy of the bone-system, presenting itself partly as a general osteoporosis, partly and principally as a typical disturbance of the growth zones of the long bones. Here the marrow loses its specific elements and gets to resemble a mucoid tissue (»Gerüstmark» or frame-work marrow of SCHOEDEL and NAUWERK). In the preparatory calcification zone the osteoblasts are lacking or have taken the appearance of spool-shaped cells of connective tissue. There is no trace to be seen of normal new bone. Infractions have often occurred, so that the bone-bridges lie scattered about in splinters — the »Trümmerfeld area». Besides fragments of bone there are also seen calcified cartilage bridges, recent and older hemorrhages and remains of such. In the cartilage the proliferating columns are in disorder. They are shorter, irregular, and the cartilage cells show degenerative changes in a higher degree than is normal. These changes often cause an enlargement of the epiphyseal line, which is specially evident in the costochondral junctions — a pronounced rosary.

If the animals that have scurvy get food containing antiscorbutic, the symptoms may be made to subside within a short time. It is easier still to get an estimation of the antiscorbutic value of an article of food, if from the beginning of the experiment a certain amount of it is given as an addition to the basal diet. The smallest quantity which then protects the animal from contracting scurvy, *the minimum protective dose*, is used as a relative standard of the antiscorbutic value of a substance. The smaller the minimum protective dose of a substance is found to be, the larger its antiscorbutic value.

In the experimental methods of Holst and Frölich, the

following investigators have proposed two modifications of principal importance.

1. The basal diet of the Norwegian authors lacks, besides antiscorbutic, also certain amino-acids, certain salts and vitamin A (McCollum, Simmonds and Pitz). However, in order to ensure reliable conclusions it is necessary to give a diet which is insufficient only as to antiscorbutic. Such a diet is proposed from several quarters and it is obvious that it may be composed in various ways.

Chick and Hume (1917) use the following: one part crushed oats and two parts of wheaten bran, and a daily ration of 50 to 60 ccm. of milk autoclaved for one hour at 120° C. According to Hess, this basal diet is so far unsatisfactory that it still retains a small amount of antiscorbutic vitamin.

Sherman, La Mer and Campbell (1922) used the following diet:

oats, whole grain	59 %
skim milk powder	30 %
butter fat	10 %
sodium chloride	1 %

The skim milk powder was heated for two hours in open dishes with access of air. After such a treatment the milk has taken a yellow colour. Avoiding to let the milk get a burnt taste and observing the variations in C-vitamin contents of the milk during different seasons, every investigator must himself ascertain — say Sherman etc. — that his technique rids the milk of antiscorbutic.

Lopez-Loma and Randoin in 1923 propose a basal diet of

white bean meal	84 %
granulated yeast	3 %
butter fat	4.5 %
calcium lactate	5 %
sodium chloride	1.5 %
paper filtrate	2 %

For preparing this food the meal is first boiled in water, and the other ingredients are then added. The authors mention that they do not use milk because it causes constipation in the animals.

These three basal diets represent the chief types that have been used. For my own part I have for practical reasons compounded a dietary in the following manner:

Crushed oats and wheaten bran *ad lib.*

60 ccm. lightly skimmed milk, bubbled through with air during 1 hour's boiling;

0,5 ccm. oleum jecoris Aselli, administered with a pipet.

The animals took this food readily until the last days of life. There remained but little of the administered quantities of oats, bran and milk. As in a few cases some animals showed an inclination for preferring oats to bran, I have in subsequent experiments, in order to be quite sure of a sufficient supply of B-vitamin, added 1 ccm. of a 50 % yeast emulsion, given with a pipet into the mouth of the animal as the cod-liver oil. — The importance of calculating the A-vitamin value of the food is evident after TOZER's investigation. Through the treatment which the milk in my diet has undergone, the A-vitamin is at least partially destroyed (HOPKINS, ZILVA, KORENCHEVSKY and CARR). The animals take the cod-liver oil readily. It had gradually become clear (HOLST and FRÖLICH, DELF, ANDERSON, DUTCHER etc., ELLIS etc.) that oxidization destroys the antiscorbutic more than heating, but that the most efficient and quickest destruction is reached by combining both. This may be done by adding hydrogen peroxide to the milk at a high temperature. That this treatment (buddization) of the milk causes scurvy in children fed entirely on such milk, has long been known to the specialists in pediatrics, at least in the North (MONRAD 1908, quoted by MEDIN). If this method is used, the hydrogen peroxide ought to be removed before feeding the animal. — Another method, used by me, is to let air be sucked through the milk during boiling. Already after half an hour of this treatment in an aëration bottle adapted for the purpose, the milk shows a light buff colour and gets a peculiar, boiled but

not burnt taste. ZILVA mentions that with this treatment the destruction of the antiscorbutic is almost complete, whereas SHERMAN etc. indicate it as being complete. According to a verbal statement of Zilva, Sherman's result is the correct one. This is also made evident from my control animals that have basal diet. As guinea-pigs in certain cases will stand milk-fat badly, I have given the milk lightly skimmed. In this manner I have not observed the inconveniences which Lopez-Loma and Randoin deem accompanying the use of milk in the basal diet.

2. The second alteration in Holst and Frölich's technique was also introduced by CHICK and HUME, and consists in using a carefully quantitative method. It can not be considered satisfactory only to place the foodstoff to be tried within the cage with the animals. On the contrary, it ought to be administered, in carefully measured rations, preferably with the aid of a pipet, directly into the animal's mouth. Only thus the guinea-pig experiment has become a biological method, comparable in accuracy to other biological methods (Hopkins).

For an examination of the antiscorbutic value of a substance to be unexceptionable, it is thus first of all necessary that the basal diet should be complete in all other respects than the antiscorbutic, and, secondly, that a quantitative procedure is adopted. Many investigations are still published (FABER 1920, HAWK etc. 1921, GIVENS etc. 1921, PEIPER 1923) where one or both of these conditions are not fulfilled. More often still the condition set forth by HESS and UNGER is neglected: a microscopic examination of the animals. Also this condition is indispensable. DELF and TOZER, who have shown that in guinea-pigs, with a diet in which only A-vitamin is lacking, certain changes appear in the epiphyses of the ribs, as a consequence forego the microscopic examination when testing the antiscorbutic value of different substances. This logic I cannot understand. The right conclusion of Delf and Tozer's investigation is, that it is necessary to attend to a fully sufficient supply of A-vitamin being present in the basal diet.

MOURIQUAND and MICHEL have published some experiments, which they consider to prove that cod-liver oil would

directly cause scurvy. They administered it in a dose of 2,5 ccm. to a basal diet of cereal and lemon juice. First of all is to be observed about this régime that it lacks certain minerals, specially calcium, as well as certain amino-acids. Furthermore, neither the changes found by the authors in the macroscopic, nor in the microscopic examination are such as to convince us that scurvy has been present. Finally, the dose of oil is so large that it may be suspected possibly to have occasioned alimentary disturbances. In sum, these investigations are ambiguous.

BEZSSONOFF reports that his experiments (1923) corroborate those now mentioned of Mouriquand and Michel about the injurious effect of cod-liver oil. The author's communications, however, do not in the least justify such an inference. The guinea-pigs in his series 9—12 do not seem to have had a sufficient ration of vitamin A, nor of vitamin C; but this can not be stated definitely as the animals do not seem to have been histologically examined. It may be mentioned that the temperature in Bezssonoff's laboratory went down below zero, which alone may have been enough to kill the animals. My series 33 and 35 show that Bezssonoff's conclusion as to the injurious influence on guinea-pigs of cod-liver oil in small dosage is not correct.[1]

That the essential conditions, in spite of their necessity, are not yet universally observed, is probably due to the slow spreading of knowledge about the fundamental investigations. Still ten years ago, experiments on the influence of different salts on the bone formation (MASSLOW) could be made without a thought being given to the antiscorbutic in the food. In the same year (1913) such a distinguished investigator as WIELAND lacked knowledge of Holst's experiments. And still in 1923 papers on infantile scurvy are published (ROSENBUND) without considering the plainest inferences which may be drawn from the study of scurvy in guinea-pigs.

[1] MOURIQUAND and MICHEL in their latest report (1923) state, that the infavourable influence of cod-liver oil is seen only when the dietary is incomplete regarding other constituents as certain salts and amino-acids.

Many authors (cf RÆBIGER) point out that the guinea-pig as experimental animal is very delicate. It requires good care, is sensitive to changes in temperature, dietary a. s. o. In the basement of my villa in Hagalund, outside Stockholm, I have arranged a well lighted room, looking South, for housing the animals by installing hot water pipes and fixing 12 wooden cages by the wall opposite the window. The cages measured 45.5 × 38.5 × 36 ccm. The whole front, which could be let down, consisted of a wire net with meshes 2.5 cm. square. In this way there was quite a uniform light on the animals. The bottom of the lowest cage was 0.5 meter above the floor. In the cages 1 to 8 animals were placed at the same time. From the point of view of infection it is advantageous to have as few animals as possible in each cage, preferably one or two. However, a comparison between my normal series and the others shows that the decisive factor for the infection generally seems to have been the lessened resistance caused by the scurvy. *Cf.* MCCLENDON etc., wo describe a pneumonia epidemic among their animals in spite of their having a cage each. My animals have been spared the great epidemics, cholera etc., which are described as not uncommon where a large number of guinea-pigs are kept.

The food basins were washed every day, sometimes every other day. The finest dry sawdust was used as litter on the tinplates covering the bottom of the cages and was as a rule changed every day, less often when pronounced oliguria was present.

As to the material, the animals were brought together from four different places, the difficulties of obtaining them all from one quarter being insurmountable at that time (July 1922 and March 1923). The animals were all of one breed, however, the so-called sleek or short-haired. Before the experiments began, the animals had full dietary from two to six weeks in order to make them recover after the transport and grow accustomed to their new surroundings, and especially learn to drink milk. In the records the animals have been drawn in their different colours. They were, as a rule, weighed every three days.

With regard to the suitable weight of the animals used for scurvy experiments, there are different opinions. COHEN and MENDEL use animals of 110—250 grams, HESS 200—300 grams, SHERMAN 300—350 grams, HOLST and FRÖLICH even bigger animals, up to more than 700 grams. It seems suitable that the weight should be between 200 and 500 grams. 174 of the present author's 189 animals had this weight at the beginning of the experiment, 14 weighed less than 200 grams, 1 more than 500.

With our deficient knowledge of the different need of antiscorbutic by the weight unit, which may be supposed to exist, a smaller animal probably wanting a larger quantity by the weight unit than a heavier one, I have thought it unsuitable to follow SHERMAN and SMITH in their calculating the dose of antiscorbutic to a uniform basis of body weight (300 grams), and I always indicate the absolute quantities directly given.

That the animals have thriven under the circumstances in question, is shown by the series 2 and 24, weight charts Fig. 96 and 118, 13 animals in all, which have had full dietary, composed of oats, bran, unboiled skim milk, swedes and green leaves, chiefly dandelion leaves. The increase in weight was satisfactory and the animals showed every sign of health till they were killed after 102—142 days. Two animals brought forth young, which in their turn developed normally. Only one animal died after 52 days; invalid after an acute tracheobronchitis, it was drowned in the milk basin. Neither this nor any of the other animals showed at the *post-mortem* examination and the subsequent histological examination the slightest sign of scurvy. The animals that were killed showed everywhere normal pictures. As controls with regard to scurvy the majority of the animals in series 3 and 25, in all 11, may also be regarded (concerning Cases 17 and 18, see below); these 11 animals, infected with a dose of tubercle bacilli, continued to increase in weight till they were killed after 102—142 days, without showing macro- or microscopical signs of scurvy. Likewise, the 16 animals in series 33 and 34 serve

as controls. Half their number lived till they were killed after 93 days, and none of them showed signs of scurvy, macro- or microscopically.

That the basal diet described above, and used by me, is free from antiscorbutic is shown by series 1 and 26, together comprising 16 animals, charts fig. 95 and 120. All these, with the exception of one who died on the first day of the experiment from an acute infection, developed typical scurvy and died after 18, 19, 24, 24, 24, 26, 26, 27, 28, 30, 31, 33, 33, 36 and 38 days respectively, with an average life-time of 28 days. SHERMAN states the average life time for animals of about 300 grams with totally scorbutic dietary to be 26—34 days, and other authors also indicate about 28 days. At the *post-mortem* examination of these guinea-pigs, all changes mentioned as typical for scurvy were present. The first scurvy symptom HESS has often been able to identify on the 12th—14th day. The earliest diagnosis was made by him on the 8th day. I have also seen CHICK's scurvy position intermediately appear on the 8th day, and in none of these cases the onset of the first symptoms was delayed longer than to the 16th day. From this I conclude that a demonstrable quantity of antiscorbutic has not been present in the basal diet. To believe, like ROBB etc. and HOWE, that the first symptom always presents itself on a fixed day and to interpret its coming a day or two later as proving the presence of antiscorbutic, is contrary to all results gained up till now. — As a careful microscopic examination of my animals has been carried out (see Records of cases), surely the basal diet fulfills the two fundamental claims, being quite free from antiscorbutic, and in all other respects a complete dietary.

The juices I have tried have been given to the animals with a pipet, graduated in 0,1 ccm. With patient handling the animals soon learn to eat in this manner, and soon they will suck the pipet as eagerly as a bottle-fed infant does his bottle, without losing a drop.

HESS has opposed the use of weight charts as scurvy charts. He admits that they often have a typical course,

when the animal only gets basal diet, with one rising and one sinking part (see Fig. 95 a. o.), but their course does not directly indicate the degree of the scurvy symptoms. Sometimes the scurvy symptoms will appear while the weight is still increasing, sometimes the weight goes down, when the animal refuses to eat or when an infection is at hand, continually from the beginning of the experiment. Hess has attempted to delineate a clinical curve. In practice, I have found this impossible. But I append the weight charts, as in any case they give much interesting information.

PART 1.

The antiscorbutic value of some vegetable products.

Survey of experiments.

The *number* is found in the Records of cases p. 174.

Diet. B. diet = basal diet (see p. 12).
For the additions, see Discussion.
M. pr. d. = minimum protective dose of antiscorbutic (see p. 10).

Weight in grams at the beginning of the experiment and after death. The signs +, —, or ? after the final weight figure indicate that the animal was not weighed at the *post-mortem* examination and that towards the end the weight curve was pronouncedly rising (+), falling (—), or level (?).

Scurvy. For the definitions, see pp. 35.
Scorbut manifestus gravior ••••.
» » mitior •••.
» latens gravior (••••).
» » extensus ••.
» » levior and incipiens •.

Table 1.

Series	Number	Diet	Weight in grams initial	Weight in grams final	Scurvy	Life-time days	Remarks
I	1	Basal diet. 0.0 m. pr. d.	250	190	****	24	
	2		270	190	****	26	
	3		270	215	****	38	
	4		260	180	****	31	
	5		295	195	****	33	
	6		275	170	****	27	
	7		270	160	****	26	
	8		275	200	****	24	
II	9		280	600	0	142	Chloroformed
	10		210	750	0	142	» , gravid
	11		270	635	0	142	» , I-para
	12		100	710	0	94	»
III	13	B. diet with swedes and green leaves. > 1 m. pr. d.	295	730	0	142	»
	14		300	710	0	142	» , I-para (twins)
	15		320	700+	0	142	»
	16		325	580	*	142	»
	17		330	780	0	142	»
	18		345	560 ?	**	142	»
	19		365	755+	0	142	»
IV	20	B. diet + 1 ccm. red whortleberry juice, 1 year old, bought at grocer's. 0.0 m. pr. d.	295	170	****	28	
	21		300	200	****	26	
	22		280	180	****	28	
	23		295	195	****	30	
V	24	B. diet + 5 ccm. of the same juice. 0.0 m. pr. d.	280	145	****	28	
	25		235	210—	****	28	
	26		290	200	****	29	
	27		285	170	****	27	
VI	28	B. diet + 10 ccm. of the same juice. 0.0 m. pr. d.	270	175	****	32	
	29		235	240	(****)	12	Died of pneumonia ac.
	30		200	140	(****)	14	Died of septicemia

Infected with tuberculosis bacilli on first day of experiment.

Series	Number	Diet	Weight in grams		Scurvy	Life-time days	Remarks
			initial	final			
VI	31		295	185	****	30	
	32		355	250	****	31	
	33		525	320	****	32	
VII	34	B. diet + 5 ccm. of raw fresh red whortleberry juice 1922. 0.0 m. pr. d.	430	210	****	38	
	35		400	255	****	35	
	36		450	240	****	43	
	37		440	250	****	31	
VIII	38	B. diet + 2 ccm. red whortleberry juice, pressed 1922 from berries preserved in water since 1921. 0.0 m. pr. d.	250	220—	(****)	8	Died of enteritis ac.
	39		265	140	****	27	
	40		270	170	****	28	
	41		275	220—	****	37	
IX	42	B. diet + 7 ccm. of the same juice. 0.0 m. pr. d.	230	175	****	29	
	43		300	180	****	25	
	44		345	220	****	26	
	45		290	205	****	30	
X	46	B. diet + 5 ccm. juice pressed 1922 from berries, stirred with sugar 1921 0.0 m. pr. d.	300	205	****	23	Died of septicemia
	47		210	175—	****	34	
	48		235	170	****	22	Suffocation
	49		270	190	****	26	
XI	50	B. diet + 1 ccm. raw juice of fresh blue whortleberries 1922. 0.0 m. pr. d.	180	155	****	30	
	51		230	150	****	29	
	52		230	155	****	29	
	53		250	180	****	28	
XII	54	B. diet + 5 ccm. of the same juice. 0.0 m. pr. d.	240	140	****	19	Died of suffocation
	55		240	175	****	35	
	56		275	185	****	32	
	57		230	170	****	23	

Series	Number	Diet	Weight in grams		Scurvy	Life-time days	Remarks
			initial	final			
XIII	58	B. diet + 5 ccm. juice from stewed blue whortleberries 1921. 0.1 m. pr. d.	210	135	***	60	
	59		275	215—	***	52	In dying condition killed with ether
	60		255	195	***	39	
	61		255	200	***	57	Died with lymphadenitis supp. subment.
XIV	62	B. diet + 10 ccm. of the same juice. 0.2 m. pr. d.	255	230	*	10	Died through overlying
	63		260	150	**	29	Died with lymphadenit. supp.
	64		255	245	*	4	Died with lymphadenit. supp.
	65		315	215	***	61	
	66		405	340	***	32	Died of bronchopneumonia ac.
XV	67	B. diet + 5 ccm. juice of fresh strawberries stirred with sugar. 0.1 m. pr. d.	240	160	***	42	
	68		280	180	***	46	
	69		255	160	***	50	
	70		285	250	***	55	
XVI	71	B. diet + 5 ccm. fir needle decoction. 0.0 m. pr. d.	370	210	****	29	
	72		380	240	****	29	
	73		445	250	****	28	
	74		360	250	****	27	
XVII	75	B. diet + 1 ccm. fresh orange juice, yet $^{29}/_{10}$—$^{18}/_{11}$ other juice. Varied value of m. pr. d.	410	260	***	46	
	76		395	390+	Healing	66	Chloroformed
	77		345	435+	»	66	»
	78		320	360+	»	66	»
XVIII	79	B. diet without ol. jec. Aselli + 2 ccm. fresh orange juice.	335	390	*	30	Died of peritonitis ac.
	80		265	260	*	19	Died of pneumonia ac.
	81	B. diet without ol. jec. Aselli + 4 ccm. fresh orange juice.	420	400—	0	60	Chloroformed
	82		480	510—	0	60	»
XIX	83	B. diet + 3 ccm. fresh tomato juice 1922. 0.1 m. pr. d.	340	200	***	43	
	84		400	280	***	39	
	85		270	230	***	39	
	86		305	225	***	43	Died through drowning

Series	Number	Diet	Weight in grams		Scurvy	Life-time days	Remarks
			initial	final			
XX	87	Oats and bran, 200 ccm. milk, raw and fresh, for them all together. 0.1 m. pr. d.	320	260	***	37	
	88		345	220	***	59	
	89		340	200	***	37	
	90		350	220	***	46	Lymphadenitis supp.
XXI	91	B. diet + 2 ccm. raspberry juice, preserved. 0.0 m. pr. d.	365	235	****	28	
	92		280	200	****	27	
XXII	93	B. diet + 2 ccm. black currant juice, preserved. 0.0 m. pr. d.	410	220	****	37	
	94		250	220	(****)	6	Cause of death doubtful
XXIII	95	B. diet + swedes and green leaves > 1 of m. pr. d.	240	270	0	9	Died at the first pipet feeding
	96		200	220	0	8	» » » » »

Summary and discussion.

Red whortleberries (Vaccinium vitis idæa, L.). Of the antiscorbutic value of these berries there is only one investigation in the literature, by FÜRST. Seven guinea-pigs were given a basal diet of oats, yellow peas and rice meal, and with this diet in all 100 ccm. red whortleberry juice (l. c. p. 148; on p. 128 the quantity of juice for each animal is indicated as 25 ccm.). The animals died after 18—28 days and all showed scurvy in a higher or lower degree. We are not told whether all the juice was consumed, and in any case it is impossible to know how much the different animals have had. Fürst believes he can conclude a certain protective effect. The conclusion is doubtful.

29 of my animals have been used for testing red whortleberries. So-called natural juice, bought at a grocer's and for the composition of which there has been no guarantee, has been tested in doses of 1, 5 and 10 ccm. Further the juice

of raw berries bought in the market-place was tested in a dose of 5 ccm.; the juice of whortleberries, which juice since 1921 had been kept in closed bottles with water poured over them, in doses of 2 and 7 ccm.; and the juice of crushed whortleberries, prepared in 1921 by stirring raw berries together with the same quantity of sugar during an hour. *All* the 29 animals showed manifest signs of scurvy; six, who died of intercurrent infection, less pronounced, the rest very marked, and died, counted in groups (the six animals mentioned are left out), after 28, 28, 31, 37, 31, 28 and 34 days, respectively. The group that had got the juice of fresh, raw berries, lived longest, which might be supposed to be due to a certain amount of antiscorbutic; but the lifetime, 37 days, is too short to allow any such conclusion.

Thus, I have not been able to prove the presence of an antiscorbutic substance in red whortleberry juice prepared in different ways. This does not preclude the possibility that a small amount may exist and under certain circumstances be demonstrated. PARSONS pointed out in 1920 that the guinea-pig, who requires a comparatively large dose of antiscorbutic, is not a very suitable animal for testing food-stuffs of low antiscorbutic value. It may be mentioned that the peasants are said of old to have regarded the red whortleberries as possessing a certain antiscorbutic value.

Blue whortleberries (Vaccinium myrtillus). Not tested earlier.

First fresh, raw juice of the year 1922 was tested in doses of 1 and 5 ccm., then juice of berries from 1921, which had been boiled and stirred for half an hour in an open pan, and afterwards kept in a closed bottle for a year, in doses of 5 and 10 ccm. *The raw juice of 1922 showed no protective effect whatever.* The animals in both series died after 29 and 27 days, respectively, in pronounced scurvy. *The boiled juice of 1921, on the other hand, showed a certain protective effect,* which for the doses given — 5 and 10 ccm. — corresponded to 0.1—0.2 of the minimum protective dose. An animal from

the first group, that had 5 ccm., died of intercurrent infection after 39 days without showing the highest degree of scurvy; the other three died of severe scurvy after an average lifetime of 56 days. Of the five animals who had 10 ccm., 4 died of infections, two very soon, two after 29 and 32 days with slight scurvy symptoms. The fifth died with pronounced scurvy after 61 days. This juice of 1921 had undergone a treatment which must be supposed to have reduced its antiscorbutic value in a high degree. As it nevertheless had proved itself so far valuable, *these whortleberries of 1921, when fresh, must have possessed quite a high antiscorbutic value.*

Strawberries. Not tested earlier.

The juice of fresh berries was given for three weeks, and subsequently the juice of berries which at the end of August had been stirred with like quantity of sugar during half an hour and then kept in a closed jar a month. *The strawberry juice showed a certain protective effect,* in a dose of 5 ccm. corresponding to about 0.1 of the minimum protective dose. One animal died with less highly marked scurvy after 42 days, the three others with pronounced scurvy after an average of 50 days.

Decoction of fir needles.

Not earlier tested experimentally on animals. The army-surgeon of Charles XII, ERBENIUS, is said to have cured »soldier epidemics» with it. TOBLER states, without indicating his dose, that he has cured scurvy in children by this means; the same thing is reported by UMBER, whereas FINKELSTEIN mentions that he has seen no clinical effect; perhaps, he adds, because the needles were not sufficiently fresh.

I tried a decoction of fir needles, prepared in the following way. The tops of fir sprigs were picked in July 1922 and kept in a cellar for six weeks; 0.5 kg. was soaked for an hour in 2 litres of water nearly 100° C. Then the decoction was strained off and bottled. *5 ccm. of this decoction showed no antiscorbutic effect whatever in four animals.* They died after

28 days. For the present it is impossible to decide whether this depended on the scanty sunshine in 1922, of which more below, or on the needles not being fresh, as Finkelstein suggests for his cases, or perhaps picked too late in the year, or whether the dose was too weak to show any effect in the guinea-pigs.

Tomatoes.

The juice of tomatoes, both fresh and sterilized, is by common consent stated to be highly antiscorbutic. A daily dose of 3 ccm. will protect a guinea-pig from scurvy. It has been proved that fully ripe red tomatoes have greater antiscorbutic value than those which are unripe and green. For my tests I used tomatoes, that had ripened late in the season of 1922. They were fully ripe but not so intensely red in colour as tomatoes may become. The juice was pressed out and was given immediately in a dose of 3 ccm. to each animal. The animals died in the most severe scurvy after an average of 41 days, which possibly may be counted as proving *a certain antiscorbutic value, but in any case very slight* (ca. 0.1 min. protective dose). In the literature I have only found one statement of failing clinical antiscorbutic effect of ripe tomatoes, and that by Finkelstein.

Milk.

200 ccm. of fresh raw milk were given during October and November 1922 to four animals, who consumed it jointly; they may have drunk different quantities. They died after 37, 37, 46 and 59 days, with pronounced scurvy. 1 litre of this milk at the least can be reckoned necessary to protect these four animals. This agrees with the experience of different investigators that milk, in itself a weak antiscorbutic, is especially weak when the cows are kept in the shed (Dutcher etc., Hess, Unger and Supplee, Barnes and Hume, Hart). The essentially different lifetime of the animals also emphasizes the necessity stated by Chick and Hume of a quantitative dosage for each animal of the substance to be tested.

Raspberry juice.

According to HOLST and FRÖLICH 10 ccm. of raspberry juice, boiled as well as raw, have a complete protective effect. I found no protective effect whatever in a liquid, bought at a pharmaceutical chemist's as »raspberry juice 1922» and given to two animals in a dose of 5 ccm.

Black currant juice.

Bought and tested under the same circumstances as the preceding, it showed no protective effect.

No conclusions must be drawn from these last experiments about the antiscorbutic value of the berries, no more than from the series with »natural» red whortleberry juice from a grocer's. But they show that it is very unsafe to rely upon berry juices and syrups bought in shops as antiscorbutic.

Orange juice.

According to various experiments (HESS), guinea-pigs require 3 ccm. of fresh raw juice to protect them completely from scurvy, while 1.5 ccm. is enough to prevent the manifestation of clinical signs (Davey).

I gave 2 ccm. and 4 ccm. of fresh raw juice and stated for the latter dose complete protection. (Series 18.) Series 17 is interesting. First the animals had 1 ccm. of raw fresh orange juice. This was pressed out of oranges that looked dry and gave but little juice; it was in October and the season was drawing to its close. The weight charts of the four animals were already declining when the oranges disappeared from the market, and therefore the animals had a dose of preserved orange juice. As this has been prepared through stirring in an open pan for nearly an hour and the antiscorbutic in the juice might thus be supposed to have lost its potency, the preserved juice was given in a dose (8 ccm.), twice as large as the one calculated to be equivalent to 1 ccm. of fresh juice. Nevertheless the animals lost weight very quickly and got worse and worse. When, after 20 days of this preserved juice, new fresh oranges were again to be had, in the month of December, 1 ccm. of fresh juice was again administered.

No. 75, who was then extremely feeble, died the next day. At first, one of the other three also showed a somewhat continued sinking of the weight curve, which is described as typical for the first days of the healing stage. Then they all rapidly recovered and grew quite lively. This series proves that even oranges may vary in their antiscorbutic value, which has been earlier pointed out incidentally by DELF, but does not seem to be universally recognized (STILL 1920).

What is most remarkable in these results, is the slight antiscorbutic power of the vegetable products of 1922. In raw blue whortleberries from this year there was no antiscorbutic value to be found, whereas it was fairly high in berries from 1921. Tomatoes, which may generally be compared to oranges, contained in the late autumn of 1922 hardly any antiscorbutic.

Raspberry juice and decoction of fir needles from the same year did not show any antiscorbutic potency either, but this may perhaps be due to special circumstances.

The reason for this marked poverty of the antiscorbutic factor in the products of 1922 can not with certainty be stated. As it has been proved that the degree of ripeness is of importance for the C-vitamin contents, and as fruits and berries ripen under the influence of the sun, it seems natural to connect the antiscorbutic potency with the sun radiance. FUNK suggests in 1922: »This original contents (of antiscorbutic) may vary with the country, in which it is produced, with the condition of the soil, the climate and so on», but the sun radiance as important factor for the forming of antiscorbutic has neither been presumed by him nor by any one else. As to the A-vitamin, it has been proved only to be formed in the light (STEENBOCK, COWARD).

If we inquire into the time of sun radiance during the late summer of 1922 in Stockholm (all the products used for the research were from the neighbourhood of Stockholm), we find it to have been as follows.[1]

[1] The figures have been kindly communicated by the meteorologist at the Public Meteorological Institution, Knut Haldin.

Table 2.

	Hours of sunshine per month: 1921	1922	Average 1908—1920
July	310	257	266
August	239	192	200
September	210	149	160

From this table we see, that whereas the figures for the time of sunshine in July, August and September 1921 were 16.6, 19.5 and 31.2 per cent., respectively, *above* the average, they were for the same months in 1922 3.3, 4, and 6.9 per cent. *below* the average. In 1921, Stockholm had an unusually sunny late summer, in 1922 it was unusually cloudy. The hypothesis about the difference in time of sunshine causing the varying antiscorbutic potency of berries, fruits and leaves, agrees well with these facts.

Conclusions.

With regard to the antiscorbutic value of the examined products, the investigation has thus shown that

1) strawberries (1922) and blue whortleberries (1921) had a certain antiscorbutic value, whereas blue whortleberries (1922) were without any demonstrable antiscorbutic potency;

2) antiscorbutic could not be detected in red whortleberries 1922, nor in decoction of fir needles of that year;

3) fully ripened, though late, tomatoes of less intensely red colour held, in 1922, but little antiscorbutic;

4) these changes in antiscorbutic value may be explained as due to different sunlight time during the ripening in different years;

5) ripe oranges vary in antiscorbutic value according to the different quality of the fruit.

PART II.

Histo-pathological studies.

Preliminary notes.

Introductory.

About the microscopic pathology of guinea-pig scurvy HESS writes in 1920: »Little has been added to the description so carefully depicted by HOLST and FRÖLICH 1907». About the microscopic pictures of scurvy in man he says, that »the study has been focussed so exclusively on the bones, that for many years, indeed until very recently, the other organs of the body were neglected». This judgment has lost but little of its validity during the latest years. Only in rare cases it is possible with absolute certainty to decide whether the changes seen in human scurvy are scorbutic or not, scurvy in man being so frequently associated with other disorders, deficiency diseases as well as infectious. It is only after experimental studies on animals that the pathology of human scurvy can be elucidated. HOLST and FRÖLICH's works are subject to the disadvantage — at that time quite natural — that in their basal diet A-vitamin and several other substances were lacking. When it comes to deciding whether microscopic changes are scorbutic, it is essential, however, that the basal diet should be complete except with regard to the antiscorbutic. This claim compels us to look at the results of most elder and many of the later investigators in the matter as being in some degree impaired by uncertainty.

For the studies in this second part of my work I have used the majority of the 96 guinea-pigs mentioned in Part I, as well as the majority of the 50 controls, which are mentioned in Part IV. For certain organs, I also use the tuberculous animals of the same series and besides 4 cases of infantile scurvy. The records of these three groups will be found in Part V.

Clinical symptoms. Macroscopic changes at the post-mortem.

I must set forth that I have found it impossible to draw a clinical curve according to HESS for the progress of scurvy. Especially the tenderness of the joints has been found too variable to form a basis for such a curve. My observations do not otherwise differ in the main from the current descriptions. With regard to the first noticeable symptoms, however, this has seemed to me most frequently to be a certain unwillingness to move, which can be observed before the changes of the joints seem to explain it and while the psychical condition still appears without fault. This weakness of muscle — for such it seems to be — is specially observed as a decreased motional effect on the guinea-pigs of a sudden and loud sound. Healthy guinea-pigs react with an instantaneous and swift movement. Guinea-pigs on scorbutic diet, that have not yet shown other symptoms, seem to perceive the sound as quickly and have an impulse to move, but the result is much less prompt than in the sound animals.

A macroscopic change that I have only found mentioned once in the literature — HART and LESSING speak of »eine Abknickung des Kopfes beider Tibien» in one of their monkeys — but which is very common in the final stage, is a deformation of the tibiae, consisting in a bending backwards of the tibia diaphyses towards the upper epiphyses. This gradually progressive curving has anteriorly a rounded outline, its axis being drawn frontally and horisontally and passing through the back of the tibia immediately below the upper epiphyseal line. It may become nearly a right angle. It renders walking extremely difficult and forces the animals to drag themselves along on their forelegs. This is the explanation of the pseudo-paralysis of the hinder half of the body which earlier investigators have mentioned and which I have also observed in these cases.

Another macroscopic change which I have not found noted in the literature, except by HOLST (»in many cases great proliferation of connective tissue across the costochondral

junction») but which is almost constant in advanced scurvy, is the appearance of certain strange connective-tissue formations on the pleural side of the intercostal musculature around the cartilage junction of the ribs, which show scorbutic changes. The shape of these formations vary. Sometimes they envelop the costochondral junction, on the upper or lower side, or both, like a rounded mould with a concave surface towards the rib and an outline merging imperceptibly into the musculature. Sometimes they appear as wedge-shaped irregular streaks, strongest at some distance from the costochondral junction. The colour is always pale grey, the surface glossy. The size varies, breadth and length measuring up to 10 mm., sometimes more, the thickness (diameter anterio-posterior) 1—2 mm. These formations only occur in advanced cases, where there is a pronounced mobility in the anterior epiphyseal lines. They are seen chiefly in the 2nd—7th interstices. This localization strengthens the supposition that they are a reaction of the connective tissue to the abnormal movements in the epiphyseal line between cartilage and bone. Accordingly, we would see here, in connection with the appearance of new joints, a periarticular connective tissue developing. This interesting formation requires a special study from a purely mechanical point of view.

Technique.

At the *post-mortem* examination, which as a rule has been undertaken on the first day after death, sometimes later, the retained parts have been placed in a solution of formaldehyd of about 10 per cent. The solution gave a faint acid reaction. The continued treatment of the preparation has been the usual. The embedding has generally been done in paraffin. The bone preparations have generally been decalcified in 5 per cent. nitric acid, some only partially, others in Pommer's solution. Frozen sections for fat staining with Weigert Htx-Scharlachrot. For the rest the stain has been Ehrlich hematoxylin-eosin, if not otherwise stated. Further, the following special staining methods have been used.

For calcium: v. Kossa (3 % silver nitrate).
» collagen: Hansen (iron trioxihematin 1 hour, after that Hansen's connective-tissue stain, according to Böhm-Oppel).
» connective tissue: Weigert hematoxylin — v. Gieson.
» fibrin: Weigert.
» elastin: Weigert and Schulz (cresylic violet).
» bone marrow, spleen: Giemsa.
» iron: ferro potassium cyanid (Berlin blue reaction) and sulphurated ammonium — ferri potassium cyanid.
» amyloid: metyl-violet.
» chondroitin sulphuric acid: methylene-blue.

In the records of cases I have indicated for each case which parts have been examined. In all over 2.000 sections have been studied for Part I and II. For want of space the detailed description of each section is not quoted in the records. only the results for different organs are summarized in the different chapters.

Nomenclature.

As denomination for the substance, the absence of which causes scurvy, I use alternately »vitamin C» and »the antiscorbutic», in conformity to most investigators. My preferring the latter, as a rule, is due to the fact that this name expresses a fundamental biological quality, the basis for the specific identity reaction of this substance. We may possibly, for want of greater chemical knowledge, as with the ferments, have to keep for a long time still to this biological nomenclature (Aron). If I have a certain sympathy for this opinion of Aron's, I must on the other hand vividly oppose his proposal to call vitamin B »ansatzfördernder» and vitamin A »resistenzerhöhender Nährstoff-Faktor». Irrespective of other nutrition factors (*e. g.* calcium), it must be emphazised that the antiscorbutic is both ansatzfördend and resistenzerhöhend. This mistake of Aron's shows better than anything how prudent those investigators have been who provisionally have fixed

a neutral nomenclature. As name of a group the word vitamin has become most widely adopted and ought to be kept till another can be found with a better chemical foundation. As to the other members of the vitamin group, for the present I use the expression vitamin A for the vitamins contained in cod-liver oil, till the question about their division into different, biologically definable substances (McCollum etc.) is further analysed. The same thing applies to vitamin B as representing the group of vitamins in yeast or bran.

Classification of scurvy in different stages.

Up to the present time scurvy has been clinically divided into a latent and a manifest stage. The first sure clinical sign constitutes the difference, which often, however, is very difficult to fix. An intermediate stage, during which suspected symptoms occur, is common and can have rather a long duration. It has been called differently: subacute scurvy (Hess); formes frustes (Lesage); abortive forms (Koch); préscorbut (Godlevski).

From a patho-anatomical point of view, there is only one attempt at classification, that of Delf and Tozer, who distinguish between five stages: »incipient, definite, acute, chronic definite, and acute chronic scurvy». This classification is deficient in many respects. The choice of the names is not a very happy one as they do not cover the meaning. The differentiating principle is not clear. Perhaps the intention of the authors was rather to single out certain types of the rib changes, than to propose a classification of scurvy in different stages.

Such a classification, however, is necessary for the discussion of the scurvy problems. As the conditions of the experimental animals, especially the patho-anatomical changes, are used for illustrating and elucidating the conditions in man, it is desirable that a common classification of the stages should be adopted, where the clinical and the physiological points of view can both have their due. An important task for the

near future is to make clear the finer physiological and pathoanatomical changes in the different stages of experimental scurvy. Only then order will be brought into the clinical findings.

In accordance with the denominations of certain earlier authors, I propose the following scheme for classification of scurvy in different stages.

- Scorbut manifestus
  - Sc. manifestus gravior
  - Sc. manifestus mitior
- Scorbut latens
  - Sc. latens gravior
  - Sc. latens mitior
    - Sc. latens extensus
    - Sc. latens levior

As differentiating principle, the clinical difference is here taken in the first place. Is there any clinical sign of scurvy, alteration of the complexion, standstill of weight, hemorrhage, typical Roentgen picture? The disease then is manifest. If clinical signs are absent, it is latent.

The second differentiating principle is physiological. Has the patient altogether been without antiscorbutic in his diet? The scurvy then is absolute or *gravior*, whether it has yet led to manifest symptoms or not. If, on the other hand, there has been a certain dose of antiscorbutic in the diet, it is a case of *scorbut mitior*, whether this has become manifest, not yet had time to develop, or possibly seems to remain latent. At the *post-mortem* examination of such a latent case, typical changes can be met with in different parts of the bone system, especially in the long bones: *scorbut mitior extensus*. Or else patognomonic symptoms are seen only in the teeth: *scorbut mitior levior*.

The physiological differentiating principle may also be made the chief principle, when the scheme will have the following arrangement:

- Scorbut absolutus or gravior
  - Sc. gravior manifestus
  - Sc. gravior latens
- Scorbut mitior
  - Sc. mitior manifestus
  - Sc. mitior latens
    - Sc. latens extensus
    - Sc. latens levior

In all cases we get the same five forms of scurvy, which shortly may be characterized thus:

1. *Scorbut gravior manifestus.*

The food has been totally lacking in antiscorbutic. This form has been the one most usually induced in the experiments undertaken so far. The changes are of a very deep-going nature and soon destructive to life. Quantitatively the patho-anatomical changes have a smaller extent on account of the rapid development of the disease.

2. *Scorbut gravior latens.*

The same thing applies to this form, which only differs from the preceding in that no clinical sign has yet become evident. This form may be divided into scorbut gravior latens *extensus, levior* and *initialis*, as is scorbut mitior latens. However, this division has not the same importance, at least not in the present work.

3. *Scorbut mitior manifestus.*

Here a certain dose of antiscorbutic has been included in the food, up to a half of the protective dose. With this lengthening of the life-time the scorbutic changes have had time to develop and show quantitatively a larger extent than in the forms indicated as *gravior*. Most cases of manifest human scurvy may be said to belong to this category.

4. *Scorbut mitior latens extensus.*

When guinea-pigs have a half to two thirds of the minimum protective dose, the scurvy generally remains latent some considerable time (for months). At the *post-mortem* examination, typical scorbutic changes are found in the long tubular bones and several other organs.

5. *Scorbut mitior latens levior.*

When guinea-pigs have had nearly the protective dose (0.8—0.9 of the minimum protective dose), there are no changes to be seen in the bone system generally; they are only found

in the teeth. The other organs show no obvious, in any case no pathognomonic changes.

About the merely functional scurvy, *scorbut initialis*[1], that is seen in the first week of scorbut gravior and may also be presumed to be a form of scorbut mitior latens, see p. 126.

In the research about human scurvy the latent forms will probably come to play a very great rôle in the near future. It is therefore of special importance to emphasize the difference between a latent case, which is only the first stage of a manifest grave illness and which is in itself severe, and the milder latent forms where the findings are different. It may *a priori* be taken for granted that scorbut mitior latens levior and initialis nowadays are the forms most common in man.

As besides the antiscorbutic dose administered also the time for which the animal has lived after the beginning of the experiment is of significance for the appearance of the changes, the reports ought to include information about the life-time, counted in days, during the experiment. For instance thus: No. 141, scorbut mitior manifestus, 0.3 min. pr. d., 52 days.

Against this proposed classification of scurvy, several objections might be raised. First of all may be said that clinically a case may one day get no antiscorbutic in the diet, and the next day a completely protective dose; and experimentally Howe has acted in this way. But such cases will hardly fit into any system. Further, the dividing of scorbut mitior latens into two groups on a patho-anatomical principle may be criticized. Any other point of view, however, is impossible to take at present, and with regard to the great importance of the latent cases I have thought this division would become useful.

Grouping of my animals within the different stages of scurvy.

In order to avoid repetition, I include here the animals infected with tuberculosis, the figures for which are printed

[1] I thus use this name for a different stage than do Delf and Tozer.

in italics. Those animals in whom an acute infection has been stated are marked with an asterisk. The average life time means the number of days from the beginning of the experiment till the animals' death.

1. *Scorbut gravior manifestus.*

No. 1, 2, 3. 4, 5*, 6, 7, 8, 20, 21, 22, 23, 24, 25, 26, 27*, 28, 31*, 32, 33, 34, 35, 36, 37, 39, 40, 41, 42, 43, 44, 45, 46*, 47, 48*?, 49*, 50*, 51, 52*?, 53, 54*, 55*, 56, 57*, 71, 72, 73, 74, 91, 92, 93, 112, 113, 115, *116**, *117**, *118*, *119*.

In all 57, of which 13 (22.8 %) with an acute infection.
Average lifetime 28.4.

2. *Scorbut gravior latens.*

No. 29*, 30*, 38*, 94*, 114*?.

In all 5, all (100 %) with acute infection.
Average lifetime 6.2.

3. *Scorbut mitior manifestus.*

No. 58, 59, 60*, 61, 65, 66*, 67, 68, 69, 70, 75, 83, 84, 85, 86, 87*, 88, 89, 90*, 121*, 122, 123*, *124*, *125**, *126*, *127**, 131*, *132*, *133*.

In all 29, of which 9 (31.0 %) with acute infection.
Average lifetime 45.2.

4. *Scorbut (mitior) latens extensus.*

No. *18*, 63*, 120*, 128*, 129*, 130*, 135*, 136*, 137*, 138*, *139*, *140*, *141*, *142**, 143*, *148*, *149*.

In all 17, of which 11 (64.7 %) with acute infection.
Average lifetime 49.4.

5. *Scorbut (mitior) latens levior and initialis.*

No. *16*, 62*?, 64*, 79*, 80*, *134**, 144, 145*, 146, *147*, *150*, 151, 152*, 153*, *155*, *156*, *157**, *158**, 159*, 160, 161, 162, *163**, *164** *165*, *166**.

In all 26, of which 14 (53.8 %) with acute infection.
Average lifetime 50.0.

6. *No scurvy.*

a) With complete dietary, No. 9, 10, 11, 12, *13*, *14*, *15*, *17*, *19*, 95, 96, 97*, 98, 99, 100, 101, 102, 103, *104*, *105*, *106*, *107**, *108*, *109*, *110*, *111*, 167*, 168, 169, 170, 171, *172**, *173*, *174*, 175*, 176*, 177*, 178, 179*, *180**, *181*, *182*, 183, 188, 189.
In all 45, of which 9 (20 %) with acute infection.
Average lifetime 82.9.

b) With relative inanition, No. 184, 185, 186, 187*.
In all 4, of which 1 (25 %) with acute infection.

c) With dietary deficient in A-vitamin, No. 81, 82.
In all 2, without acute infection.

7. *Healing scurvy.*

No. 76, 77, 78.
In all 3.

CHAPTER I.

The bone formation in scurvy. (Figs. 1—51.)

The opinion asserted in recent years, that the bone formed in the course of scurvy, before the total arresting of bone formation, is normal bone, proves to be incorrect. It is shown that in scurvy a bone is formed, the appearance of which differs more and more from the normal, till all bone formation stops. This less differentiated bone is described in teeth, in endosmal and enchondral bone formation. Quotations from the literature show that earlier investigators have observed and described these formations, though, as a rule, they have misinterpreted them.

Teeth.

A closer analysis of the changes in the teeth in scurvy. The statements of earlier writers are completed, rectified or confirmed.

Historical notes.

»That macroscopic changes take place in the teeth by guinea-pig scurvy has been noted by many investigators. The teeth become somewhat yellow, lose their glistening appearance and occasionally break off. The molars commonly become loosened, so that they can readily be removed from their alveolar sockets; less frequently, this is true of the incisors.» (HESS.) In 1916, JACKSON and MOORE held they had found, »that with marked changes in the teeth there was often great dilatation of the veins in the pulp attended by more or less hemorrhage, and that in guinea-pigs, fed on oats and hay, there was almost complete necrosis in the pulp of the molars». ZILVA and WELLS (1919) were the first to give details about the microscopic changes. They studied teeth of guinea-pigs and monkeys. Unfortunately, the illustrations in their work are such as to make it necessary for us to confine ourselves exclusively to the text. According to this, a fibroid degeneration of the pulp sets in. This kind of degeneration which up till now has been attributed only to inflammatory causes, would thus here for the first time be shown to be due to a dietetic cause. In the pulp of the scorbutic teeth there is, according to these writers, »no trace of interstitial cement substances. Nerves, cells, blood vessels, odontoblasts, are no longer recognizable, right up to the apex of the root. The change appears to start first in the odontoblastic cells at the top of the pulp, working down towards the apex followed by distended blood vessels and hemorrhage. Then complete fibroid degeneration follows». They also state, that »the tooth is one of the first, if not the first part of the system to be affected by the deficiency of antiscorbutic material in the diet». In 1921, E. F. ROBB, GRACE MEDES, MCCLENDON, GRAHAM and MURPHY published a study of scurvy and its bearing on the preservation of the teeth. They have »sectioned teeth of quite a number of guinea-pigs and always found marked changes, if antiscorbutic was not included in the diet. The changes in the teeth proper were surprising. There was marked hy-

peremia of the pulp, with some hemorrhage. The odontoblasts lost their tall columnar form and secreted osteodentin very rapidly. The osteodentin nearly filled up the cavity in some cases». P. Howe has during the last years after experiments on a large scale, intended to make clear the effect of diet upon the teeth, published a number of incomplete and rather fantastic communications and figures. He induced scurvy in guinea-pigs and monkeys by giving them a diet, free from antiscorbutic, and only now and then, when manifest symptoms of scurvy had developed, giving them a dose of orange juice, which he does not indicate exactly, only it was large enough to prevent the animals from dying. As a consequence of this, Howe finds pyorrhea alveolaris developing, and also a process which he considers homologous with caries dentium in man. Part of the teeth of Howe's guinea-pigs have been examined histologically by Toverud, who describes them as follows: »The normal orthodentin is largely substituted by osteodentin, which, incorporating degenerated odontoblasts, reaches far down towards the apex of the tooth. There is only a very narrow space of orthodentin surrounding it. *The pulp tissue is so degenerated that one can scarcely recognize any of its normal elements. In the more severe cases there is nothing at all left of the proper pulp tissue, only some degenerated odontoblasts*[1], which may be seen scattered around. In many cases there seems to have been a fatty degeneration.»

In chemically examining the scorbutic teeth Toverud found a decreased calcium proportion and an increased proportion of magnesium.

That is all I have found in the literature upon the subject. The criticism will be given in discussing my own results.

Own investigations.

I have examined the lower jaw of 150 of my guinea-pigs. The section has been made frontally, at right angles to the

[1] The italics are mine.

longitudinal axis of the lower jaw through the middle of the foremost molar on each side. (Figure 1.) Hereby four teeth have been reached in each section. There has been a longitudinal section of the molars and a cross section of the incisor roots running inside and below these, one on each side. The topography of such a section is shown in Figure 2. For the interpretation of the sections I have collaborated with a dental surgeon, Dr. Gösta Westin. He is at present occupied in an intensive study of all my guinea-pig jaws in series of sections and will report on them as well as on continued experiments with own material. The result of my investigation, therefore, is given here only in broad outline. Embedding in paraffin has been found not very suitable for the study of summary pictures, as the molars and the jaw-bone are easily frayed. On the other hand it is more advantageous than celloidin sections for the study of the cells and the finer structure.

A normal picture from guinea-pig teeth is shown in Fig. 3, Case 188, as well as in Cases 9, 10, 11, 12, 13, 14, 15, 17, 19, 95, 96, 189.

An incipient scurvy is noticeable in the tooth already 8 days after the starting of absolute scurvy diet. The first change affects the odontoblast layer. This layer which forms the intermediate link between pulp and dentin, has normally a very regular structure of long, slender, parallel cells with processes into the dentinal tubules. In scurvy this regularity is broken, and at the same time a hyperemia appears in the pulp. The parallelism of the odontoblasts becomes less pronounced. At intervals more rounded, osteoblast-resembling cells are seen in their stead. In these places the corresponding part of the predentin seems to have lost the protoplasm processes from the odontoblasts. It lacks Tomes' canals and seems amorphously calcified. (Fig. 4, 5, 7, Cases 29 and 38.) In the dentin, however, which was already calcified at the onset of the scurvy, Tomes' canals seem to remain, and here they are widened (Fig. 5). Inside the calcified dentin, which re-

sembles an amorphous cement, a hard tissue is deposited in the course of the process, stained blue-grey by hematoxylin (Fig. 6, Cases 29, 79, 80). In the place of the odontoblasts, at the inner, notched edge of this tissue, osteoblast-resembling cells are seen. Similar cells are also seen further in towards the centre of the pulp (Case 63) and in different places the above-mentioned hard tissue reaches into the pulp in diversiformed strands, surrounded by osteoblast-resembling cells (Fig. 7 b, Cases 4, 18, 20, 21, 23, 24, 25, 35, 48, 49, 50, 54, 57, 59, 60, 66, 67, 83, 86, 87). These strands or columns already from the first show a certain regularity in their arrangement, standing radially in relation to the centre of the pulp. They are early connected by transverse columns and show a distinct bone structure (Fig. 8, 9). In sections prepared by grinding (Sonnenburg) we have verified that this is calcified bone. In Fig. 9 and 10 it is also seen that the pulp has become rich in osteoblast-resembling cells, which between them have islets of homogeneous, eosinophile tissue. This tissue is supplanted in the next stage by calcified bone, which thus may occupy most of the former space of the pulp (Fig. 10, Case 58, 88). Thus part of the pulp tissue, osteoblasts, other pulpa cells and vessels are enclosed within canals, which partially are very narrow, containing in a cross section one single cell, resembling a bone corpuscle, or a capillary, while others are wider, resembling Haversian canals (Fig. 11 and 12). Thus, the character of this pulpa bone is spongy and porous. In longitudinal sections of molars (Fig. 13) it is seen how this new bone formation is already strongly developed in the parts of the pulp which are next to the crown, whereas it is still weak at the open root apex.

In the development described above, dilated veins show in the pulp (Fig. 6, 8, 9), and more or less rounded or oval spaces (Fig. 9, 10), which give the impression of a hydrops ex vacuo. In some places there are hemorrhages, generally few and small.

The extent of this new growth of pulpa bone seems to depend on the course of the scurvy. In cases where the pro-

gress is rapid, there being no antiscorbutic substance in the diet, the bone formation is often reduced to a thin layer next to the calcified predentin with only small columns, or none, growing into the pulp (Fig. 14, 15, 17, Cases 1, 23, 50). If, however, there has been a small amount of antiscorbutic in the food, which has somewhat lengthened life, but not precluded the fatal issue, the bone formation is more vigorous. In the former group of cases we sometimes find the picture of a lively resorption of pulpa bone. In the pulp large hydropic spaces appear (Fig. 15, 17) and the thin lamella of newly formed pulpa bone lying close to the dentin is perforated by numerous lacunæ, filled with cell-syncytia, »osteoclasts» (Fig. 16). There is no trace of any odontoblasts, and the remaining osteoblasts resemble spool-shaped cells of connective tissue.

If the animals, however, after a time of scorbutic diet, receive a life-preserving daily dose of antiscorbutic substance, the development becomes a different one. Series 17, animals 75—78, is an instance of this. See weight charts, Fig. 111. In Case 75, that died of mitigated scurvy, we find the bone formation very vigorous right in towards the centre of the pulp (Fig. 18). When the three other animals in the series had had orange juice added to their diet, recovered and had been killed, we see the pulpa bone reorganized to irregular dentin (Fig. 19, 20, 21). Slender odontoblast-like cells appear again, even if they are not at once as regularly arranged as in animals which are sound from birth. The bone columns are perforated by Tomes' canals, running irregularly. This irregular dentin possesses at the same time bone canals with cells and bloodvessels, and dentin canals, and it may therefore rightly by called osteodentin.

The stage of development of the pulpa bone may be somewhat different in animals fed on the same dietary, and corresponds to the differences in the progress of the scurvy. As examples may be quoted the animals 1 and 3 in Series 1. The former died first of the eight animals in the series. The pulpa bone does not seem to have been developed in any high degree. In any case the resorption has soon predominated,

and at death only inconsiderable rests are to be seen. Animal No. 3, which died last in the series, 13 days after the first, shows the pulp to a large extent filled by pulpa bone. If the changes thus may differ in degree in different animals fed on the same dietary, they seem in nature closely to correspond within each group.

This interpretation of the connection between the different pictures presented by the sections from my 97 first animals, is confirmed through the study of the teeth in those animals which have received a carefully titrated dose of antiscorbutic, consisting of 0.1, 0.2, 0.3, 0.5, 0.7, 0.8, and > 1.0 of minimum protective dose (m. pr. d.). The changes are seen in Figs. 22—30 and may be shortly summarized as follows.

0.1 m. pr. d. Fig. 22. Highly widened Tomes' canals in the old dentin. The new formation, reaching towards the centre of the pulp, consists of bone.

0.2 m. pr. d. Fig. 23. Highly widened Tomes' canals in the old dentin. The new formation, reaching towards the centre of the pulp, consists of bone, in the outer (oldest) part of which there is seen a trace of Tomes' canals.

0.3 m. pr. d. Fig. 24. The same picture, but with a less distinct widening of the dentinal canals in the old dentin and less pronounced formation of bone in the pulp.

0.5 m. pr. d. Fig. 25. Widening of Tomes' canals not very distinct in the old dentin. The new formation consists of dentin and bone. The dentin closes round the old dentin, is lighter in colour than this, has an irregular inner edge and an irregular odontoblast layer. The bone is seen in two symmetrical places to reach in towards the pulpa centre.

0.7 m. pr. d. Fig. 26 and 27. Similar picture.

0.8 m. pr. d. Fig. 28 and 29. No distinct change of the old dentin. The new formation consists entirely of dentin, of a lighter colour, with irregular inner edge and disturbed odontoblast layer. Hyperemia in the pulp.

>1.0 m. pr. d. Fig. 30. Normal tooth picture. Well arranged odontoblast layer, predentin and dentin of normal appearance. Possibly some hyperemia in the pulp.

Fig. 26, compared to Fig. 27, and Fig. 28, compared to Fig. 29, show that it is not so much the time during which a guinea-pig has had scurvy, as the antiscorbutic dose it has received, that is determinative of the tooth picture. In the first couple the animals have received 0.7 of the minimum protective dose during 22 and 92 days respectively. The tooth picture is principally almost identical. In the latter couple an antiscorbutic dose of 0.8 has been given during 29 and 92 days respectively. The tooth pictures are principally identical and well defined from that of the first couple. This amazingly sharp difference between groups, where the difference of antiscorbutic dose is only 0.1 of the minimum protective dose, is in most cases invariably found.

Such is the picture of the changes in the teeth in scurvy, which the study of the sections have given to me and Westin. It gives no reason for altogether accepting the descriptions and explanations offered by earlier writers. But on the other hand we have been able to verify certain details of their investigations. Like ZILVA and WELLS, and TOVERUD, we have found that the changes are very early, that they begin in the crown part of the pulp and spread towards the root. These changes, however, by no means consist of »a total fibroid degeneration». A few cells may degenerate and die, the odontoblast layer as a regular, creeper-like covering of the inner even surface of the dental bone may disappear and necroses occur in the pulp. In the place of the odontoblast layer we see in any case cells appear with continued activity, real osteoblasts, and an active new formation of bone instead of dentin sets in. In no case we have been able to find a picture where the term fibroid degeneration with reason can be applied to the scorbutic changes in the teeth, nor have we found any case, where such changes affect the whole of the pulp, so that »no trace of cellular organization can be found anywhere». It is remarkable that Zilva and Wells among their illustrations, moreover rather indistinct, do not show any one that can be interpreted in that manner. The one among our sec-

tions, which most resembles one of their pictures, is an oblique section of a longitudinally cut molar, in which the pulp centre has not been reached (Fig. 31). But even here, it is not necrosis but newly formed bone.

Robb etc. have approached the right explanation nearer than Zilva and Wells. They interpret, as has already been mentioned, the »fibroid degeneration» of those two writers as a formation of osteodentin, secreted by the odontoblasts. By the term osteodentin, however, we evidently ought to understand a tissue which mainly possesses the qualities both of bone and dentin. The hard tissue formed in the pulp of the teeth in fully developed scurvy resembles bone, but it lacks the constitutive quality of dentin, Tomes' canals. Nor can the formation of pulpa bone be ascribed to odontoblasts, as the bone-forming cells are not like those but look like osteoblasts. There is certainly a great probability that the regular odontoblast layer is changed into irregular strings of osteoblasts. But Robb etc. give no details of these changes described by us. On the other hand, the name of osteodentin may with reason be applied to the irregular dentin, which is formed when the scorbutic pulpa bone, after the recovery of the animal, is reorganized by the reappearing odontoblasts (an observation, not described by Robb and his colleagues), and to the dentin, formed in scorbut mitior latens.

Howe does not seem himself to have undertaken any histo-pathological examinations, and those of Toverud, mentioned above, are very summary and, as is shown, in part incorrect.

We recapitulate and summarize the changes in the teeth produced by scurvy, as we have interpreted the pictures, in the following manner.

1. *The gradual change of the odontoblast layer.* This seems to be a sure sign of scurvy and one of the earliest changes to set in. The odontoblasts assume another shape, grow shorter, more rounded, and show another arrangement, the normal regular, creeper-like formation makes way to a layer, which in some places curves in towards the centre of the pulp

and is soon split through the cells secreting a hard tissue between themselves, so that the syncytial character of the cell layer does not plainly appear. The odontoblasts have been transformed into osteoblasts placed in bone canals. Incidentally may be pointed out how well this process agrees with the conception of the syncytial character of bone which Professor G. Häggquist has lately expressed in the Society of Swedish Physicians.

2. *The amorphous calcification of the predentin.*

3. *Widening of Tomes' canals in the dentin formed before the onset of scurvy.*

4. *New formation of bone instead of dentin.* This bone is first lying as a thin layer inside the calcified predentin, but soon extends reticularly towards the centre of the pulp. This bone has a spongy, porous character.

5. *Dilatation of vessels and in early stages hyperemia; sometimes hemorrhages in the pulp.*

6. *Atrophy and resorption of pulpa tissue*, pulpa cells, the newly formed bone and the old dentin. This resorption, which, as everywhere in bone formation, will surely be found also with scurvy in all stages, appears more distinctly after all the new bone formation in the final stage has stopped, and may proceed so far, that in the place of the pulpa tissue there is seen nothing but some large hollows filled with fluid.

7. *In the healing of the scurvy* — at an earlier stage — *reorganization of the pulpa bone into irregular dentin, osteodentin*, with bone canals and dentinal canals.

8. *In a scurvy which is latent all through or very much mitigated*, when at least half the amount of antiscorbutic needful to an individual is provided — forms which are the most common in man — *the progress is similar, though not so pronounced and presents pictures, that differ considerably less from the normal.* If the antiscorbutic dose provided is 0.5—0.7 of the minimum protective dose, an irregular dentin is formed with Tomes' canals in most places, but in the lingual part of the pulp there are found in some symmetric places ridges of a hard tissue, with the character of bone and lacking dentinal

canals. In this pulpa bone as well as in the newly formed irregular dentin, there are canals of Havers' type and isolated bone corpuscles which may be considered to consist of transformed odontoblasts. (Fig. 25—27.)

With an antiscorbutic dose of 0.8 or more of the minimum protective dose, the picture here described is changed so far, that there is no pulpa bone, but all the newly formed hard tissue in the pulpa consists of osteodentin (Fig. 28, 29), or even dentin (the first formed layer).

The endosmal bone formation.

A new interpretation is given of the changes found by earlier investigators in man and monkey, which correspond to those found in guinea-pig by the present author.

Fraenkel has described and drawn the roof of the orbit in a child suffering from scurvy. He shows how the side of the bone next to cerebrum seems normal, with vigorous bone lamellæ, parallel mutually and with the surface, while the surface towards the orbit looks quite different. Instead of the vigorous columns, parallel with the surface, here we find slender columns standing at right angles; the illustration which is given bears a striking resemblance to Fig. 10. The periosteum is thin, and instead of lymphoid marrow there is framework marrow. Hart and Lessing describe the condition of the lower jaw of monkeys suffering from scurvy. They make »die interessante und wichtige Feststellung, dass auch am Unterkiefer Veränderungen nachzuweisen sind. Die Corticalis des Unterkiefers bietet ein ganz zerfressenes und zernagtes Bild» — »ein verwittertes Aussehen. Die Auflösung des Knochens erfolgt aber nicht nur von aussen, sondern namentlich auch von den Haverschen Kanälchen, die breit eröffnet sind, in denen ein feines zellarmes fibrilläres Gewebe wuchert.» In all their cases periosteal hemorrhage was present. They also report »die poröse, zerfressene Aussenfläche des Schädeldaches». The descriptions of earlier authors are summarized thus by Hart and Lessing: »Die Bildung jungen periostalen

Knochengewebes ist von BARLOW, BAGINSKY, SCHMORL, SCHOEDEL und FRAENKEL gesehen worden, und von letzteren drei Authoren auch mikroskopisch studiert worden. Über die von Schoedel geäusserte Ansicht, dass diese Knochenneubildung keine primäre Erscheinung sei, vielmehr in die Reihe der Heilungsprozessen in weiterem Sinne gehören, herrscht volle Einigkeit.» HART and LESSING agree with this interpretation and attach special importance to the hemorrhages, which KOCH had already done. The investigators of recent years who have occupied themselves with the jaw in guinea-pig scurvy, characterize the jaw simply as »decalcified» (HOWE, TOVERUD, ROBB etc.).

I have studied the endosmal bone formation above all in the sections before mentioned under the heading of »Teeth». My pictures (see Fig. 10, 33, 34) recall those described by the investigators just named, more especially FRAENKEL, and HART and LESSING. The number of my cases being large, it is obvious that these changes — osteoporosis in the jaw, new formation of a porous, spongy bone on the surface instead of the usual, compact — are constant, as soon as the scurvy has reached a certain degree. In all cases where scorbutic changes have been manifest in the epiphyses of the long bones, they are also evident in the jaw. The new formation of this spongy bone is by no means uniform, it reaches its maximum in the lower ridge into which the roots of the molars penetrate. The new formation of this bone is on the section seen to begin along a straight line. In most sections there is no periosteal hemorrhage. The marrow is frame-work marrow, very deficient in cells. Stained with hematoxylin-eosin this spongy bone turns blue and is calcified. In cases where the bone formation seems to have stopped, it shows pictures of resorption with »osteoclasts» (Fig. 34).

A bone of the same appearance will sometimes be formed, when some special reason sets in for increased activity of the periosteum in the diaphyses of the long bones. This is, for instance, the case when, as sometimes happens, a fractured bone

wall has been thrust into the marrow cavity and the periosteum forms a bone of the above mentioned character on the outside. (Fig. 35, 43, 45.)

Thus the endosmal bone formation in scurvy of an early stage seems quantitatively as well as qualitatively to be reduced. From this there follows in the first place an osteoporosis, the more pronounced the more the scurvy has advanced, and with that a new formation of a calcified bone of spongy character, which is seen especially in certain definite sites (places of rapid growth) and which grows more slowly and gets more porotic the further the process advances.

The enchondral bone formation.

The detailed descriptions by earlier investigators of the scorbutic changes in the epiphyses of the long bones are quoted, especially in such portions that have been interpreted in a new manner by the author's own research and have now for the first time got an acceptable explanation. Already from those descriptions it may be supposed, what is confirmed through this research, that in scurvy a bone is formed enchondrally which is less differentiated than the normal bone and of a quite dissimilar character. This bone has been described by some investigators without further explanations, by others it has been interpreted as necrotizing after fracture, by others again, and this is the general explanation of recent years, as fibrin.

The macroscopic changes are described by SCHMORL and FRAENKEL in the following words: »Verarmung der Diaphysenenden an Knochensubstanz, Verbreitung der präparatorischen Verkalkungszone.» Further particulars are given by HART and LESSING: »Die schmale und scharfe weissgraue Linie der präparatorischen Verkalkungszone sehen wir ersetzt durch eine wechselnd breite, diaphysenwärts nicht ganz scharfe, weissgraue Zone von mürbem, morschem Aussehen, von dem Schoedel sagt, man habe beim Zufühlen mit der Messerspitze die Empfindung, als wenn sie aus lauter kleinen kalkhaltigen Körnern bestände.»

I give the following extracts from descriptions by some

authors of the microscopic changes in this preparatory calcification zone.

JACOBSTHAL 1900:

»Als neuer Bestandtheil treten schmale, unregelmässig umgrenzte, bucklige, verkalkte Bälkchen auf. Sie sind stalaktitenähnlich, anastomosieren zum Theil; fast durchweg sind sie vollständig kalkhaltig.» Sometimes the central parts are colourless. Uncalcified substance is only met with in a few places and to a small extent. »Die Verkalkung ist eine homogene. In ihrem Innern erhalten die beschriebenen Gebilde Knochenkörperchen, die etwas grösser und plumper gebaut sind als die des normalen Knochens, doch zeigen sie bei Luft-Injection ziemlich reichliche, zum Theil anastomosierende feine Fortsätze.»

SCHOEDEL (1900) has described in an exceedingly clear and apt manner the changes seen in cases of scurvy in infants within the bone formation zone of the long bones. He has also proved that the strange formations to be seen there, are bones. This demonstration of his seems to have been forgotten, as ASCHOFF and KOCH do not appear to know it. On the other hand, Schoedel's explanation is less plausible when he declares the unusual character of the bone to be a necrosis consequent of fracture, at the same time stating that a fracture is not always present. The description is found *l. c.* pp. 33, 37, 38, 39, 40, 41, 44, 56, 57, 62, 63, 64, 65, 79, 85, 93, 98, 104, 111, 112, 122, 133, 134, and 135. It may be summed up thus:

Next to the cartilage proliferation zone there follows a wide greywhite zone, which under the point of the knife gives the impression of consisting in nothing but small grains of calcium. In this zone there are seen a large number of bone columns, often irregularly layered, often transversely. They are bulky, thick, massive, and their majority is seen subperiosteally. Often processes, or a network of processes, continue from these columns well into the marrow. These bone columns show none or few bone corpuscles. Often remaining calcified cartilage substance is seen in their centre. Schoedel regards these bone columns as more or less necrotic and believes the necrosis to be a consequence of the fracture which »*in most cases*» can be observed.

These columns are often connected with a tissue of a different appearance which Schoedel describes in the following manner:

»In mit Hämalun-Eosin gefärbten Präparaten ist eine eigentümliche, glänzend rubinroth gefärbte schollige Substanz auffällig. Sie ist immer im Anschluss an Knochen- oder Kalkbälkchen zu finden, u. z. liegt sie dann stets innerhalb der die Bälkchen umgebenden Osteoidsäume. *Fast immer*[1] sind diese Schollen an Stellen gelagert wo anscheinend Fracturen oder Zertrümmerungen solcher Bälkchen eingetreten sind. Hier und da findet man auch, der fraglichen Substanz benachbart, blassbläulich oder blassrosa, schmutzig verwaschen gefärbte Schollen, die ebenfalls in osteoide Substanz eingeschlossen sind. Ein Bild machte besonderen Eindruck: Ein kleines von einem breitem Osteoidsaum umgebenes Knochenbälkchen ist in der Mitte quer gebrochen, die beiden Enden sind etwas an einander vorbeigeglitten, ohne jedoch dabei den Osteoidsaum zu durchbrechen, und jedes trägt nun eine kleine Haube dieser rubinroth gefärbten, glänzenden, scholligen Substanz.«

»Wahrscheinlich handelt es sich um verändertes Knochengewebe, welches nicht selten allmählich in diese Substanz übergeht. Zuweilen sind Knochenkörperchen darin enthalten, deren Kerne mangelhaft gefärbt sind. Auffällig ist das gehäufte Auftreten fraglicher Massen in den seitlichen Partien des Schnittes.«

»Osteoide Substanz ist nicht mit den rubinroth gefärbten Stellen zu verwechseln, da sie nur eine zarte Hellrosa-Färbung angenommen hat.«

»Grosse, schon mit der Lupe bequem erkennbare, unregelmässig gestaltete, bei schwacher Vergrösserung structurlose, meist gleichmässig roth gefärbte schollige Massen — — — es laufen von ihnen bandförmige Ausläufer aus. — — — Damit dürfen in der gleichen Zone gelegene Gewebelücken nicht verwechselt werden, die mit einem feinflockigen, schwach roth gefärbten Inhalt ausgefüllt sind und die offenbar nichts anderes als Gerinnungsmassen darstellen.«

Schoedel has the impression that this homogeneous tissue, stained ruby red with eosin, consists of transformed calcified cartilage or bone columns. In epicrises and discussion he does not speak about them, but emphasizes that the disturbances in the bone formation are »weniger leicht verständlich». In

[1] The italics are mine.

summarizing he indicates them as being a »Hemmung, ja vielleicht ein Stillstand der Ossification».

HART and LESSING, 1913:

»Angrenzend an die verkalkte Knorpelgrundsubstanz finden wir zunächst nun ganz kurze, auffallend plumpe und dünne, nun gelegentlich kleine Reste verkalkter Grundsubstanz einschliessende Knochengebilde ohne jede Orientierung der Lagerung, meist quer zur Knochenachse, und dazwischen allenthalben Herde krümeliger rötlichblauer Massen, die wohl nichts anders als zerfallende Kalkbälkchen darstellen. Den Knochenbälkchen fehlt grossentheils ein deutliches Osteoblastenlager, und wo Osteoblasten nachweisbar sind, sind sie niedrig.»

»Die Blutmasse traumatischer Blutungen bildet, wenn sie älter ist, zusammen mit nekrotisiertem Gewebe und einem Kalkdetritus jene eigentümlichen, fibrinösen Massen, von denen SCHMORL zuerst berichtet hat. Auch wenn sie keine grössere Trümmer von Kalkbälkchen einschliessen, haben wir ihnen Riesenzellen, zuweilen in beträchtlicher Anzahl, anliegen sehen, dagegen ist es uns manchmal selbst an offenbar recht alten derartigen Herden aufgefallen, dass keine Zeichen von Pigmentbildung wahrzunehmen waren.»

»Wenn JACOBSTHAL aus dem Gerüstmark unregelmässige Knochenbälkchen entstehen lässt, so müssen wir demgegenüber schon hier erwähnen, dass im floriden Stadium der Möller-Barlowschen Krankheit dem im Diaphysenmark wachsendem Gewebe, also dem Gerüstmark, die Fähigkeit der Knochenbildung vollständig abgeht. Nur im Heilungsstadium begegnen wir ihr.»

INGIER (1913) speaks, in a description of the changes in the primary calcification zone of scorbutic guinea-pig ribs, about bone splinters, lying embedded within a homogeneously coloured, structureless mass. This is mentioned in many places, and she seems to look upon it as consisting of fibrin, detritus etc. She points out as remarkable that the bone splinters embedded in this mass do not show any apposition, and sums up the bone changes as an atrophy of the bone with completely arrested bone formation.

ASCHOFF and KOCH (1919) describe this eosinophile mass in the calcification zone as fibrin.

»Das Trümmerfeld ist regelmässig gegen den Knorpel zu durch Fibrin abgedeckt, welches sich sofort einstellt, auch wenn der kleinste Bruch besteht, und sich als Schutzschicht zwischen Knochen-

trümmer und Knorpel einschiebt. Dass dieser Schutz des Knorpels gegen Reibung die Hauptaufgabe des Fibrins zu sein scheint, zeigen alle mikroskopischen Präparate mit grosser Regelmässigkeit. Man sieht durchweg, wie nur die Knorpelseite der Knochentrümmer, soweit kleinere Splitten nicht ganz in den Fibrinmassen liegen, von dem Fibrin bedeckt wird. Letzteres pflegt sich auffallend stark mit Eosin zu färben, enthält nur selten Blutbeimengung, ist vielfach stark hyalinisiert und kann natürlich auch Zeichen der Organisation aufweisen». (P. 89.)

»Woher dieses Fibrin kommt, ist nicht leicht zu entscheiden, da es nicht den Anschein hat, als ob es aus grösseren Blutungen in dem Bruchspalt stammte; sonst müsste unter den vielen zur Untersuchung gelangten Rippen[1], die alle Stadien der Frakturierung umfassen, sich sicher auch solche gefunden haben, wo man neben Fibrin noch frisches Blut in grösseren Mengen im Bruchspalt liegen sieht. Das ist aber durchaus nicht der Fall, sondern Blutungen im Bruchspalt treten ganz zurück. Nur kleine Reihen roter Blutkörperchen sieht man in einzelnen Fällen in das Fibrinnetz eingeschaltet.» (P. 85.)

From page 54 to page 80 in the authors' record of cases, the description of this »fibrin» is met with on every page, and the investigation has been accepted by Hess, who quotes it in several places, just concerning the »fibrin» (*l. c.* p. 106, 108, 109).

Herzog (1921) describes similar pictures in guinea-pigs as Aschoff and Koch of »rötlich gefärbte, auch Fibrinfärbung gebende, nekrotische Massen zwischen dem Knochen und Knorpel». He altogether agrees with the opinion of the above-mentioned authors that these masses are fibrin, acting as a kind of protection.

Against this interpretation Iwabuchi, in 1922, makes a cautious opposition: »Die Ansicht von Aschoff und Koch, dass die Fibrinmassen als Schutzschicht des Knorpels gegen die Reibungen der freien Knochentrümmer aufzufassen sind, trifft wohl nicht für alle Fälle zu, denn ich fand Fibrin, einige zarten Knorpelspangen der enchondralen Ossificationszone umhüllend auch dann, wenn es noch nicht zur Kontinuitätstrennung und Trümmerfeldbildung gekommen war».

[1] In all, 14.

Author's remark.

Several of the authors mentioned lay stress upon the difficulties of interpreting the pictures described in this manner. These difficulties specially arise in the explaining of the strongly eosinophile coloured columns or masses which connect cartilage and bone (SCHOEDEL), or are seen in layers on the surface of the bone bridges which faces the cartilage (ASCHOFF and KOCH), or completely enclose splinters of normal bone (INGIER a. o.). — SCHOEDEL's explanation of them as being bone, necrotizing as a consequence of fracture, fails through the fact that there sometimes is no fracture (ASCHOFF and KOCH, IWABUCHI, the present author). Aschoff and Koch who call the formation in question fibrin are not able to explain from where this fibrin may have come.

As a result of studies of more than 1 000 ribs and a large number of the other long bones from guinea-pigs suffering from scurvy, I am able to give another explanation which solves the difficulties. In the majority of these ribs there are formations like those described above, and a detailed description would largely be a repetition of the quotations I have given (Fig. 35—48). My investigation shows that the formation in question, as Schoedel moreover has already proved, is *bone*. That this bone gives fibrin colour, is not surprising, as it has this quality in common with all other bone. The fibrin colouring is not specific. In the sections I have been able to follow the forming of this bone in its different phases. In early stages it is seen like a net of somewhat irregular columns to join the cartilage columns with the normal bone bridges. They show canaliculi, even though these are fewer in number and not so regular as normally. In later stages the formative power seems to be lost more and more, and the osteoblasts, now spool-shaped and slender, surround almost structureless masses, in which only some few canals with an enclosed cell or red blood corpuscle suggest bone structure (Fig. 37—40). These masses are often connected both with the normal bone columns and with the calcified cartilage columns, which, in conformity with FRAENKEL's description, grow further inwards than normally. Sometimes we see, between the eosinophile

bone and the cartilage columns, columns of basophile bone, in the centres of which the primarily calcified beams of the cartilage remain. A darker colouring of an added surface layer and the elongated cells (osteoblasts) next to this, justify in some measure the term of bone (Fig. 43). Finally there are seen in some cases, as ASCHOFF and KOCH have described, decaying granulous masses without structure. These are probably to be considered as a secretion product of the now impotent osteoblasts, a last desperate attempt at bone formation. At last all ossification stops, and all the different kinds of bone now described become subject to resorption.

With regard to the chemical conditions of this bone, we have shown on sections prepared by grinding of not decalcified ribs, with side light according to SONNENBURG, that it is here a question of calcified tissue. The same thing appears from staining with silver, according to v. Kossa (Fig. 41), and from radiograms (Fig. 42), taken by Dr. Å. ÅKERLUND, which show the pathognomonic appearance, first described by FRAENKEL, of a dense shadow in the preparatory calcification zone, shading off linearly towards the epiphysis, diffusely towards the diaphysis.

By staining the collagen substance according to HANSEN it is shown that this bone, formed in the course of scurvy, lacks collagen fibrils. (Plates 1 and 2.) While the collagen assumes a beautiful red colour with this staining, the bone in question turns yellow, in the same manner as the precollagen in embryonal bone tissue. In the cartilage the collagen in scurvy is considerably weaker than normally.

An other sign indicating the abnormal character of the scorbutic bone is that rests of the preparatorily calcified cartilage substance, which has not been organized, remains for a long time visible in the bone columns. This has already been pointed out by SCHOEDEL a. o.

The enchondral bone formed in the cource of scurvy thus differs from the normal bone chiefly in the following points:

1. The osteoblasts more and more assume the appearance of elongated connective tissue cells.

2. The regular form of the normal bone and its general organisation are lacking.

3. The typical bone structure, with bone corpuscles and canaliculi, becomes less and less apparent; instead of that there is a general homogenization of columns and masses.

4. Collagen fibrils are absent.

Among the circumstances which have seemed to earlier investigators difficult of explanation, but which well agree with the interpretation given here, I may mention the following:

That »Knochenkörperchen» (SCHOEDEL) are seen in the eosinophile tissue in question.

That this tissue is always seen in connection with bone or cartilage (SCHOEDEL) and that it most frequently covers the portion of the columns which is turned towards the cartilage (ASCHOFF and KOCH).

That this tissue is seen between cartilage and normal bone even where there is no fracture (IWABUCHI). ASCHOFF and KOCH also found that 2 of the 14 ribs investigated were without fracture, and in one of these two they saw the so-called fibrin formation.

That fissures traverse this tissue (HART and LESSING).

That in cases of coincident rickets this tissue was always found enclosed in osteoid seams (SCHOEDEL).

That it is fretted by giant-cells (HART and LESSING, a. o.); this is a question of resorption pictures.

That it lacks pigment (HART and LESSING), which would be unaccountable if we suppose, like those authors, that it originates from hemorrhage.

That bone columns enclosed in such masses always lack apposition-picture (INGIER); this is natural, as these masses themselves constitute the apposed bone tissue.

That this inferior bone is most frequently found where there is a fracture, is explained by the circumstance that, in a certain stage of scurvy, the ribs — for it is chiefly in the ribs that this coincidence is observed — are nearly all fractured, as already HOLST and FRÖLICH have noted in 1912. In the other long bones the tissue described is seen more frequently

in unfractured bone. Even in ribs I have observed the same thing in several cases. Where the fracture occurs, it is probably in certain cases partly due to such inferior bone having replaced the normal bone. For example, see Fig. 43, where the fracture has occurred unusually high up in the diaphysis, and just in an accumulation of that kind of bone. If, which is possible, a fracture can call forth a formation of this special bone as a callus formation, surely the relation of cause and effect can also be the opposite: the fracture occurs in consequence of the qualitative as well as quantitative inferiority of the bone formed in the course of scurvy.

The rows of red blood-corpuscles that ASCHOFF and KOCH have seen in the »fibrin net», seem to have been capillaries between the bone bridges.

Aschoff and Koch, as well as Hart and Lessing, also have illustrations which as far as they go — though not so well as the descriptions — confirm the conception that is expressed in these pages.

It also agrees well with the interpretation quoted, that, as H. WINBERGER has found in 1922 by Roentgen-examining scurvy patients, »die mächtigen Schattenkeulen an den distalen Femurmetaphysen an ihren epiphysären Rand eine enchondrale Ossification im Sinne eines normalen Längenwachstums zeigen»; that is, the direct connection of the shapeless bone masses formed in scurvy with the preliminarily calcified columns of the cartilage, displayed in the histological sections by Schoedel and the present author, has been stated by Winberger already during life by aid of Roentgen rays. Winberger did not pronounce on the importance of his discovery in his preliminary communication.

The microscopic changes, about which I have entered into particulars here, are situated in the preparatory calcification zone and the so-called »Trümmerfeld area». With regard to the macroscopic appearance of this zone, »the white line» and the formation of a typical rosary, as well as the occurrence of the frame-work marrow or »Gerüstmark» and of a general osteoporosis all through the long bones in scurvy, these changes,

as earlier writers have described them, have also been constant in my cases and are most marked in the 2nd—8th pairs of ribs. Concerning these I will therefore only enter into one small detail.

ASCHOFF and KOCH write in their records of cases (p. 80) — speaking of the rib in which no fracture could be discovered: »Bei der 6:ten Rippe verdient noch hervorgeheben zu werden, dass sich *im Fugenwinkel an der Aussenseite*[1] unter dem Perichondrium Fibrinauflagerung findet und dass auf dieser umschriebenen Stelle das Knochenmark zellärmer aussieht». The case in question is an early stage of scurvy. This most frequent site of the first scorbutic change in the bone marrow and bone (Fig. 37, 44, 45) is described by several authors ever since HOLST and FRÖLICH in 1912 (see Fig. 3 in their work), who explicitly associate it with the quicker growth in this place. The parallelism between the formation of frame-work marrow and pathological bone, of which Aschoff and Koch give such a good example, I have found constant in all my scorbutic guinea-pigs. The more the bone marrow loses its specific character, the less the osteoblasts also resemble the normal, and the more pathological the new bone becomes till finally the bone formation ceases. It seems to me most natural to consider this a matter of co-ordinate changes of bone marrow cells and bone cells.

How the inferior bone formed in scurvy develops when the disease is remedied, is found from Series 17, animals 75—78, Figures 45, 46, and Plates 1 and 2. Animal 75 died of scurvy and showed great changes in its bones with abundant formation of scorbutic bone (Fig. 45 a and b, Plate 1). The other three animals in the series also had severe scurvy, but the day before the death of the first they were given a dose of orange juice and recovered. After a month they were killed. The bone picture is seen from Fig. 46 a and b, and Plate 2. The osteoblast layer has resumed its normal appearance, so has the bone marrow. The cartilage columns have not yet become fully arranged. The bone columns consist for

[1] The italics are mine.

the most part of newly formed bone, differing from the normal in a certain bulkiness of structure and in having strong bone columns running transversely, just like the scorbutic eosinophile columns. Remains of these are seen, some lying between the new columns, in which case a strong resorption seems to take place, some lying enclosed within them. That it takes a long time before the calcification zone in scurvy altogether returns to the normal state, has been proved by Roentgen examinations of children (FRAENKEL, FRANK). Still 17 months after the clinical recovery, scurvy could be diagnosed in the radiogram. It is important in such examinations, however, that attention should be paid to the antiscorbutic dose given, in order to make sure that there is a complete recovery and not only a passing of the scurvy from a manifest to a latent stage, as is possibly the case in Series 17.

Cartilage.

The atrophic changes in scurvy of the proliferating zone of the cartilage are well known after the descriptions of previous investigators. As a new thing I have in scurvy cases found a collagen atrophy in the cartilage. This collagen atrophy is especially marked in the columns of the proliferating zone and in their neighbourhood. The sections stained with methylenblue do not indicate any difference from the normal in regard to chondroitin-sulfuric acid.

Four cases of infantile scurvy.

The conception of the bone structure in scurvy which has been pronounced above after experiments on guinea-pigs, I have been able to corroborate by reference to descriptions and illustrations by earlier writers on the pathology of scurvy in infant and adults, in guinea-pig and monkey. I have also had the opportunity myself of studying a large number of sections from 8 cases of scurvy in the first and second year

of life, examined *post-mortem*, prepared and described by Professor U. QUENSEL in 1898. Professor Quensel has most kindly handed over the material, which later on will be published by us more exhaustively, to enable me to communicate some extracts.

Four of these cases belong to the 15 cases of morbus Barlow, recorded by MEDIN at the Northern Congress for Medicine in Kristiania 1899. An abstract of Medin's lecture is to be found in Norsk Mag. f. Laegevid., 59, 1899, p. 1016. The following extract may be quoted:

»A similar disease has not been described from the Allmänna Barnhuset during the late 55 years, when the first case occurred in January 1898. The second followed in June, and during the whole year in all 5 cases. During January—May 1899, 10 cases appeared. The age of the patients was $^1/_2$—1 $^1/_2$ year. They were all weak children, fed with cow's milk, *all of them with chronic intestinal catarrhs.* Twelve of the children had rachitis, two lues. The first symptom was the change in the general condition, the complexion becoming greyish pale. The children lay still, displayed tenderness when touched. The extremities were swollen, especially at the epiphyses. Hemorrhages in the muscles, periosteum, and gums, even before dentition. Four cases led to death.» (*Post-mortem* record, see below.)

MEDIN agrees with the English and Americans that morbus Barlow is infantile scurvy. The differences extant are explained by the anatomical and physiological circumstances in the growth of the child. Medin points out, that out of his 15 cases 3 lacked clinical signs of rickets. Of these 3, one had been carefully examined patho-anatomically without any trace of rickets being found.

The general death rate in 1897—1898 among the children at the Allmänna Barnhuset is said to have been lower than at any earlier period. The milk had since 1887 been sterilized with Soxhlet's apparatus. In this manner 5—6 000 children had been fed without any scurvy appearing previously. During the last years the children had been given Mellin's food, up to 8 teaspoonfuls a day, and milk-sugar. The treatment consisted of administering the juice of $^1/_2$—1 lemon daily.

Among these 8 cases, of which patho-anatomical examination has been made, rather exhaustive records have now been

found concerning 4, from which records extracts are given in Part V.

These records show beyond doubt that the four children were suffering from infantile scurvy. In four more children who during the same time had died in the Allmänna Barnhuset from intercurrent diseases, Quensel found typical scorbutic changes which I have studied in his microscopical sections, Fig. 49—51. Quensel's exceedingly careful histological examination allows us to follow the formation of scorbutic bone in its different phases. First the bone cells lose their canaliculi. Then the bone cells themselves become scarce, and a homogeneous calcified bone is formed, in which there are few or no corpuscles. In cases complicated with rickets, the osteoid tissue shows the same structural changes towards a structureless tissue. Even in small details, such as the higher degree of the rib changes on the outer, convex side, and the first formation of the scorbutic bone occurring in the »Fugenwinkel», the changes present in Quensel's cases correspond to those found by me in guinea-pigs.

When, in an institution with uniform dietary for a large number of persons, cases of manifest scurvy appear, it is generally found on closer investigation that many of the others also show symptoms that may be suspected to be of scorbutic nature. In order to investigate whether this was the case in the Allmänna Barnhuset at the end of the nineties, I have closely gone over the cases described by QUENSEL in his book of 1899. Quensel has brought together extracts from clinical and *post-mortem* records about 144 children, mainly in the three last quarters of the first year of their life, who died during the time June 1895—October 1897 and were examined by him from a different point of view (the presence of bacteria in various organs). The scorbutic symptom which is most easily identified subsequently is the hemorrhagic diathesis, and I have tried to ascertain the presence of this symptom. I found that, out of the 144 children, 73 showed hemorrhages during the last months of their lives or at the *post-mortem* examination. The organs which have been affected have been the follow-

ing (I leave out of consideration one case, which has been diagnosed as scorbus infantilis and stands as No. 1 among those reported above): dura mater as a pachymeningitis hemorrhagica interna 37 times, cerebrum 1, lungs 23, pleura 7, pericardium 2, palate 1, tonsils 1, oesophagus 1, ventricle 1, intestine 11, cutis and subcutis 17, middle ear 3, kidneys 3, ureters and bladder 4, conjunctiva palpebrar. 1, lymphoglandulæ mesent. 1; besides, blood was found during life in fæces 7 times, urine 4, vomits 1, secretion from nose 6. Blood in the renal canals was found 7 times at the microscopical examination. — In all 139 localizations.

All the 144 children in question had infections and in a large number of cases culture of bacteria, in most cases streptococci, was made with inoculation on animals. Only 2 cases formed a basis for assuming that the bacteria were actually hemorrhagiparous. In both cases it was a question of bacillus pyocyaneus, which caused intestinal hemorrhages in rabbit.

I certainly do not intend to express as my opinion that scurvy in *every* case should have been the cause of the hemorrhages here mentioned. In some cases (QUENSEL's Cases 12, 60, 84), however, it is possible with great probability to draw the conclusion that clinically fully developed but unidentified *manifest* scurvy has been present. For the majority of the remaining cases the supposition of an otherwise latent scurvy seems to be the natural explanation of such a frequent hemorrhagic diathesis (50 %). From this we might conclude that the cow's milk which was given in the Allmänna Barnhuset during this time was scorbutogenetic. The appearance of a series of manifest cases, as recorded by MEDIN, is partly explained through this, but to make the explanation complete we require the evidence of a circumstance, likely to aggravate the scurvy in these cases. This circumstance is given in Medin's information that all the children, who had manifest scurvy, suffered from chronic enterocatarrhs. From many different quarters it has been pointed out that these catarrhs often call forth an outbreak of scurvy, both in children and adults (see p. 117). It may also be remarked that SCHOEDEL (l. c., p. 119)

considers Mellin's food to have contributed to the appearance of scurvy in one of his five cases. Of this food the children in the Allmänna Barnhuset were given up to 8 tea-spoonfuls a day.

Summary and conclusions concerning the scorbutic bone formation.

Concerning the bone formation in scurvy, HOLST and FRÖLICH write in 1912: »Eine Apposition von normalem Knochengewebe scheint ganz zu fehlen». About a formation of pathological bone they say nothing. HESS summarizes in 1920 the investigations undertaken up to that time thus: »In scurvy osteoblastic bone growth is greatly inhibited, but what growth does take place occurs in a normal and orderly manner». The investigation reported above shows this conception to be wrong.

Before the total cessation of growth after a guinea-pig has been put on absolutely scorbutic diet, at least two, often four weeks elapse. During this time a less differentiated bone is formed in teeth as well as in endosmal bones and the epiphyses of the long tubular bones. This pathologic bone can be seen in the teeth already during the course of the second week, in the lower jaw and ribs during the third week. If there is any antiscorbutic contents in the food, the formation of this bone goes on for a longer time and it gains a larger extent. The bone-forming cells change in appearance. The odontoblasts take the character of osteoblasts, the osteoblasts grow more and more like spool-shaped connective-tissue cells. In the teeth and the lower jaw the new pathological bone has, instead of the ordinary, compact, a spongy, porous character. Also the diaphyses of the long bones become porous. At the epiphyseal junctions, on the other hand, shapeless, dense column masses are formed instead of the slender spongy net-work of bone. In teeth and lower jaw the pathological bone contains collagen fibrils even though they are less developed than in normal bone; in the new columns of the long bones collagen substance is lacking. This pathological bone is everywhere calcified. There is no evidence for the *bone*

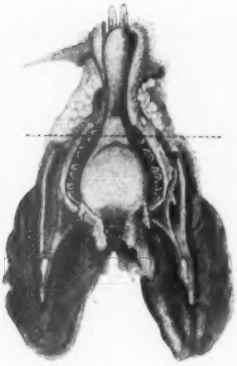


Fig. 1. Location of the section at right angles to the longitudinal axis of the lower jaw through the middle of the first molar.

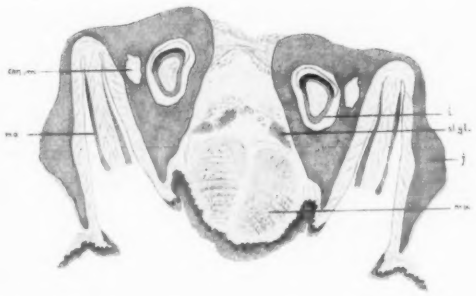


Fig. 2. Diagrammatic section through the lower jaw.

j jaw-bone, *mu* muscles of tongue, *sl gl* glandula sublingualis, *i* cross section of root of incisor., *mo* longitudinal section of molar, *can m* canalis mandibulæ with vessels and nerves.

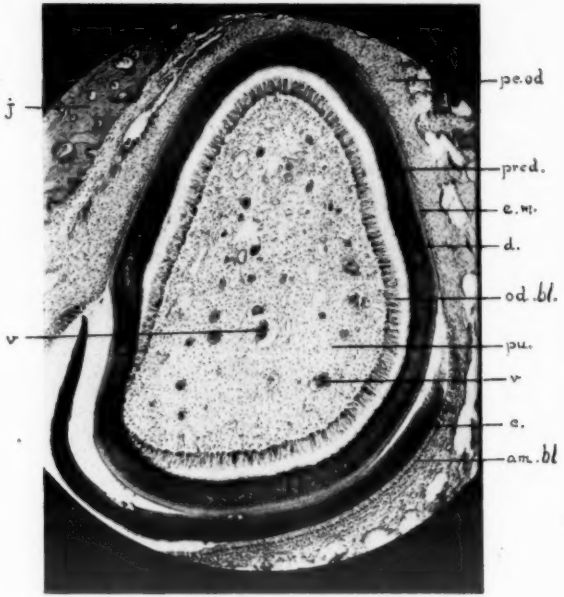


Fig. 3. No scurvy. No. 188.

Cross section of normal incisor. Low power.

j jaw-bone, *pe od* periodontium, *c m* cement membrane, *d* dentin, *pred* predentin, *od bl* odontoblasts, *pu* pulp, *am bl* amyloblasts, *v* bloodvessels, *e* enamel.

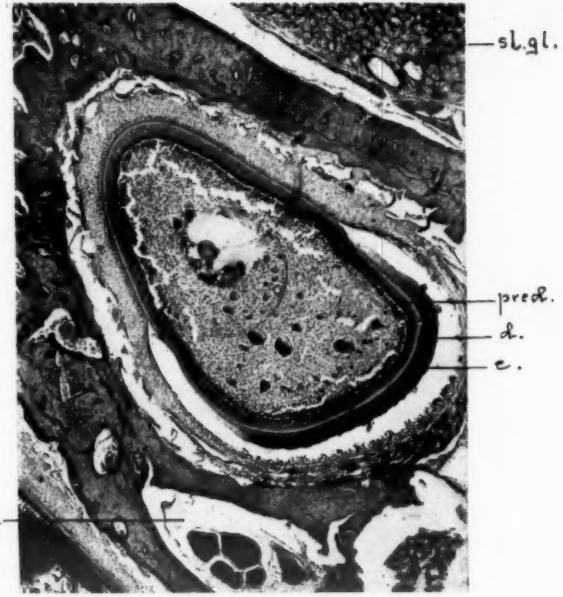


Fig. 4. Scorbut latens gravior, 8 days. No. 38.

Cross section of incisor. The predentin *(pred)* is amorphously calcified.

d dentin, *e* enamel, *sl gl* sublingual gland, *c m* the widened canalis mandibulæ.

am amyloblasts, *v* bloodvessels, *e* enamel.

canalis mandibulæ.

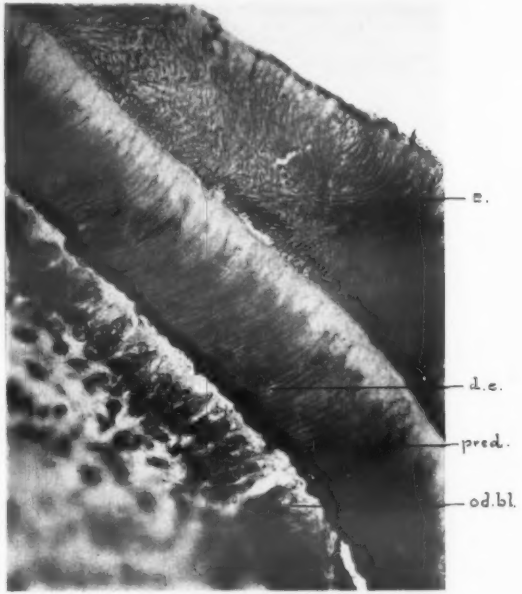


Fig. 5. Scorbut latens gravior, 12 days. No. 29.
Predentin *(pred)* amorphously calcified, Tomes' canals *(d.c.)* widened. Odontoblasts *(od bl)* in disorder.
e enamel.

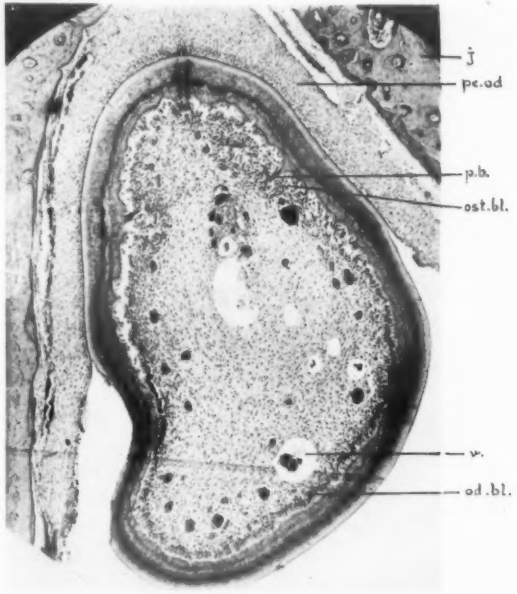


Fig. 6. Scorbut latens mitior. No. 18.
Cross section of incisor. Bone *(pb)* growing into pulp
ost bl osteoblasts, *v* dilated vein, *od bl* odontoblasts in disorder, *pe od* periodontium, *j* jaw-bone.

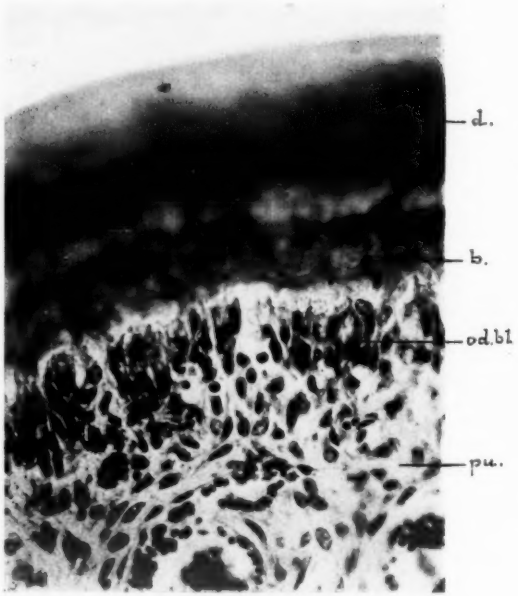


Fig. 7 a. Detail of Fig. 6, from the oral side of the incisor

od bl odontoblasts in disorder, *b* hard tissue, looking like amorphous cement, *d* old dentin, *pu* pulp.

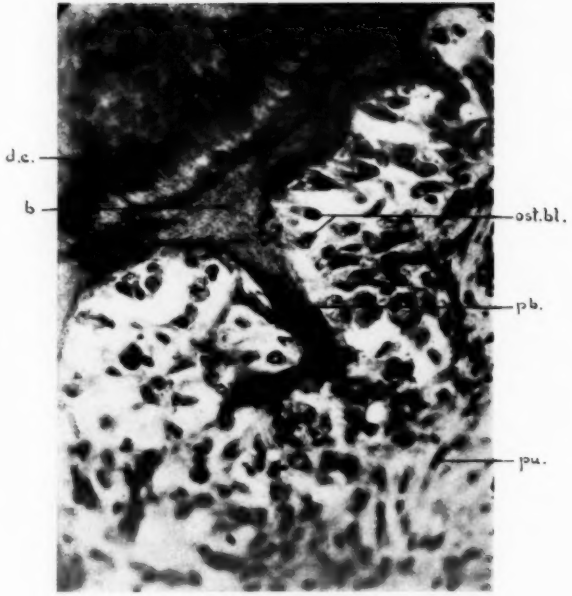


Fig. 7 b. Detail of Fig. 6 from the opposite side to Fig. 7 a.

ost bl osteoblasts, *pb* pulba bone, *dc* old Tomes' canals, widened, *pu* pulp, *b* amorphous bone.

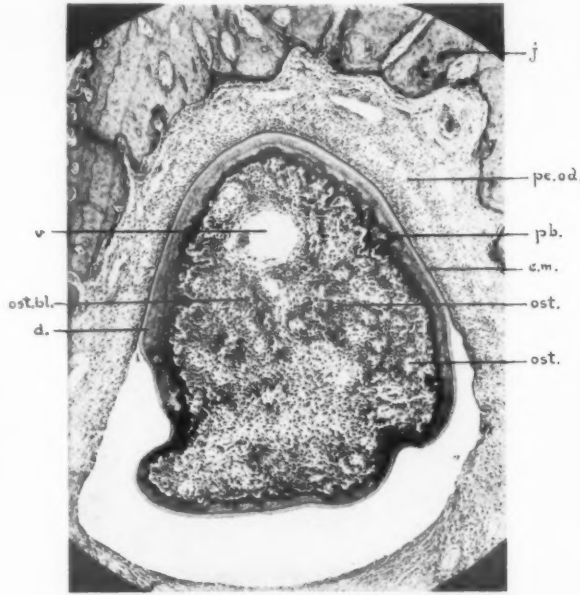


Fig. 8. Scorbut mitior manifestus. 0.1 m. pr. d., 60 days. No. 58.

Cross section of incisor. Low power. Osteoblasts *(ost bl)* fill the pulp. Between them a homogeneous substance, osteoid *(ost)*.

pb pulpa bone, *d* dentin, *c m* cement membrane, *pe od* periodontium, *j* jaw-bone, *v* dilated vessel.

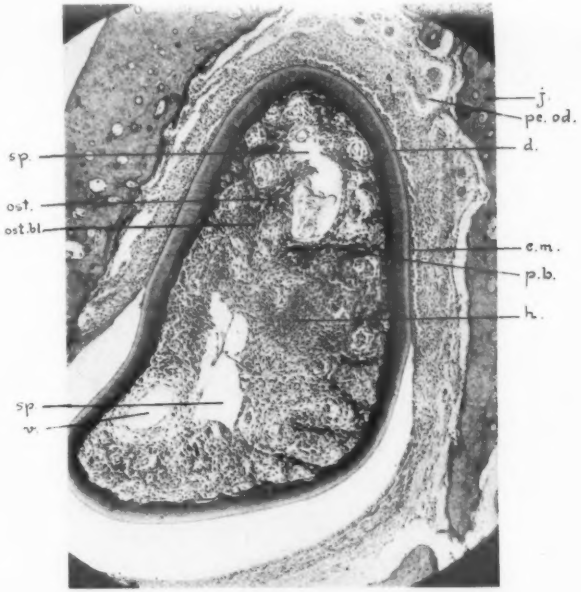


Fig. 9. Scorbut manifestus gravior, 28 days. No. 25.

Cross section of incisor. Low pover. Bone *(pb)* growing into pulp. Osteoblasts *(ost bl)* fill the pulp. Between them osteoid *(ost)*.

sp hydropic spaces, *v* dilated vein, *h* hemorrhage, *d* dentin, *c m* cement membrane, *pe od* periodontium, *j* jaw-bone.

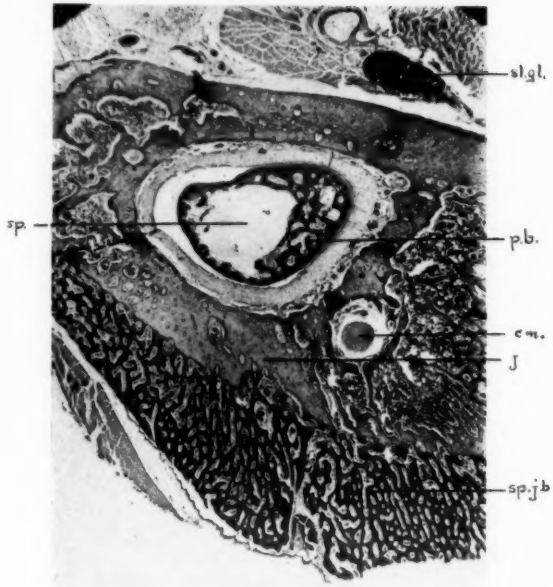


Fig. 10. Scorbut manifestus mitior 0.1 m. pr. d. 59 days. No. 88.

Cross section of lower jaw. Formation of bone of spongy character in the pulp *(pb)* and on the outside of the jaw *(sp jb)*.

c m canalis mandibulæ, dilated, *sp* hydropic space, *sl gl* sublingual gland, *j* old jaw-bone.

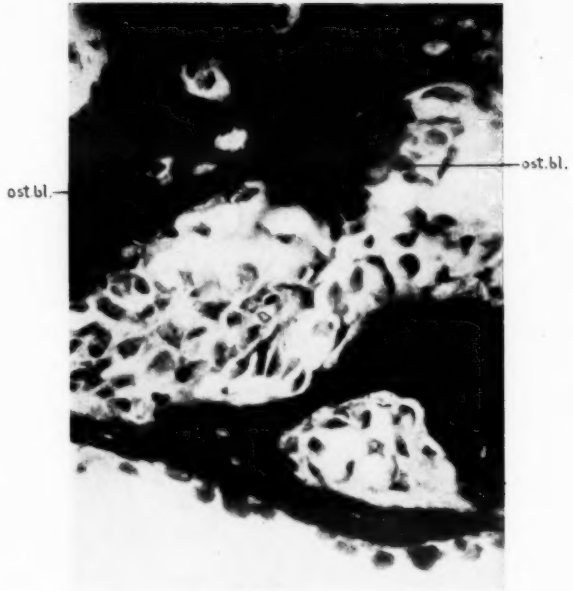


Fig. 11. Detail of Fig. 10 (high power), showing the canals in the porotic pulpa bone.

ost bl osteoblasts.

c m canalis mandibulæ, dilated, *sp* hydropic space, *sl gl* sub-lingual gland, *j* old jaw-bone.

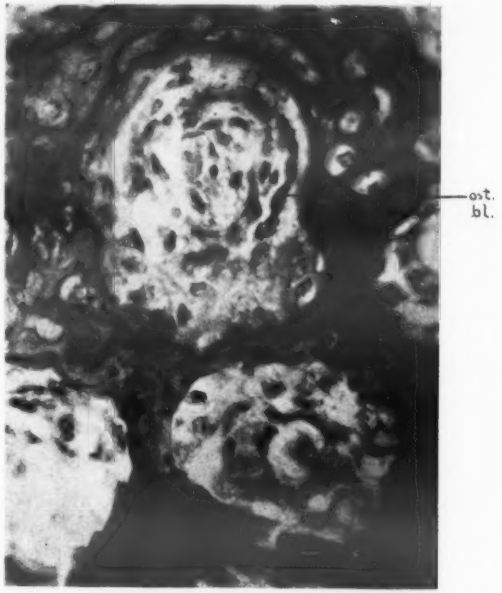


Fig. 12. Scorbut manifestus gravior, 23 days. No. 57.

Longitudinal section of molar, high power, showing the canals in the spongy, porous bone.

ost bl osteoblasts.

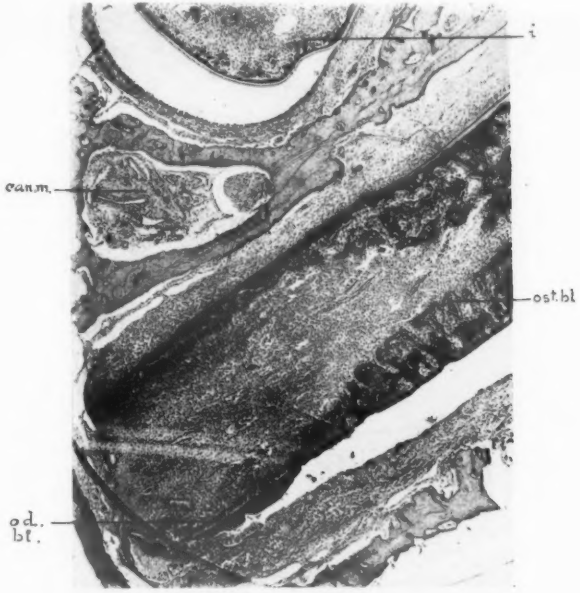


Fig. 13. Same as Fig. 12, low power.

The pulpa bone gets stronger the more it approaches the crown.

od bl odontoblasts, *ost bl* osteoblasts, *can m* canalis mandibulæ, dilated, *i* incisor.

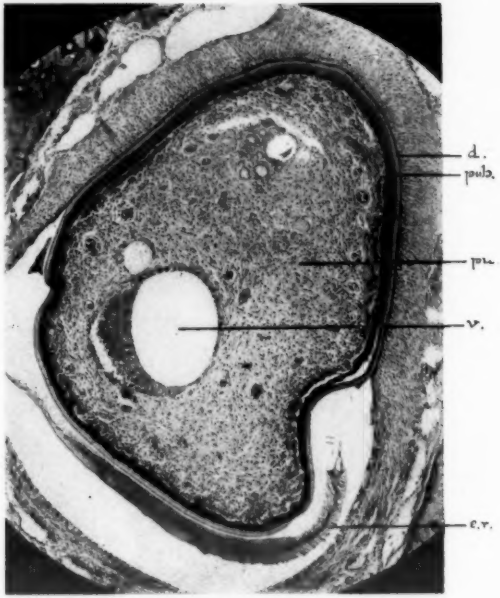


Fig. 14. Scorbut manifestus gravior, 24 days. No. 1.

Cross section of incisor. Low power. Slight layer of pulpa bone *(pb)*.

pu pulp, *d* dentin, *e r* remains of enamel, *v* dilated vein.

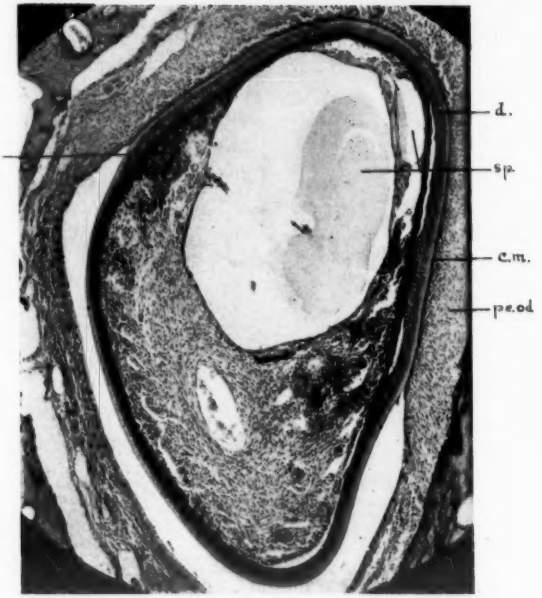


Fig. 15. Scorbut manifestus gravior, 30 days. No. 50.

Cross section of incisor, low power. Resorption of pulpa bone.

pb [illegible]

c m cement membrane, *pe od* periodontium.

pu pulp, *d* dentin, *r r* remains of enamel, *v* dilated vein.

c m cement membrane, *pe od* periodontium.

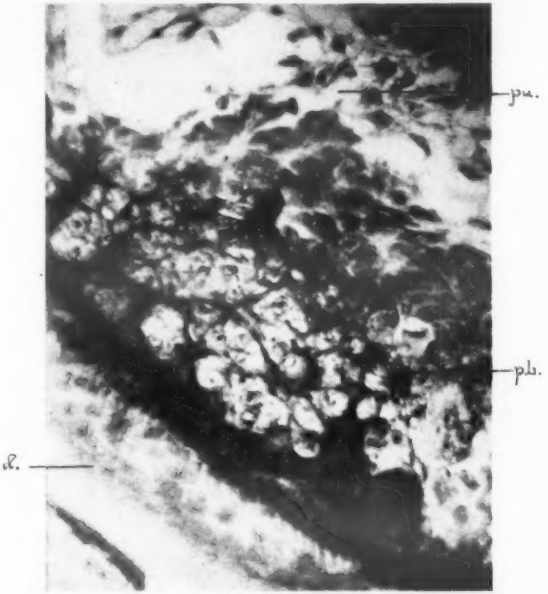


Fig. 16. Detail of Fig. 15, high power.
pb remains of pulpa bone bridges, *d* dentin, *pu* pulp.

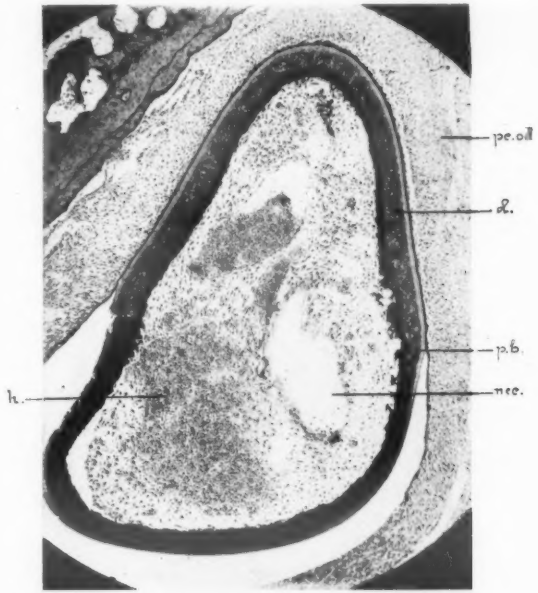


Fig. 17. Scorbut manifestus gravior, 30 days. No. 23.
Cross section of incisor, low power. Resorption of pulpa bone *(pb)*.
h hemorrhage, *nec* necrosis, *pe od* periodontium, *d* dentin.

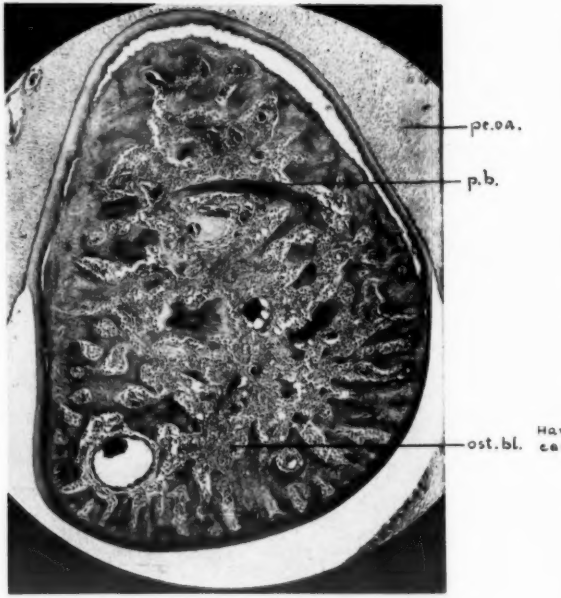


Fig. 18. Scorbut manifestus mitior, 46 days. No. 75.

Cross section of incisor, low power. Pulpa bone *(pb)* fills the pulp.

ost bl osteoblasts, *pe od* periodontium.

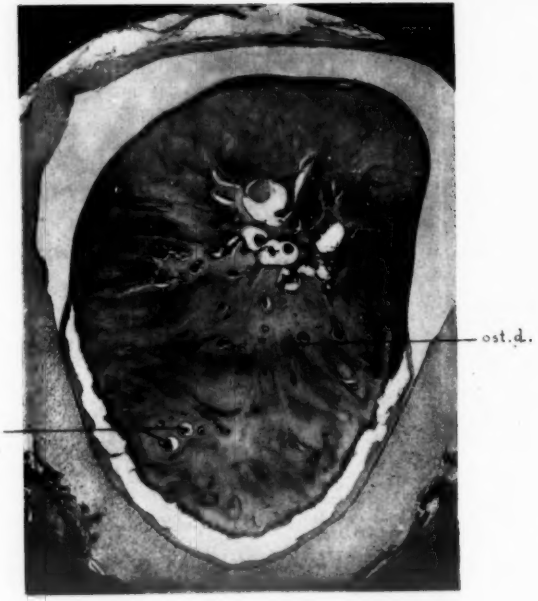


Fig. 19. Healing scurvy. No. 76.

Cross section of incisor, low power. Osteodentin *(ost d)* fills the pulp.

Hav can bone canals.

ost bl osteoblasts, *pe od* periodontium.

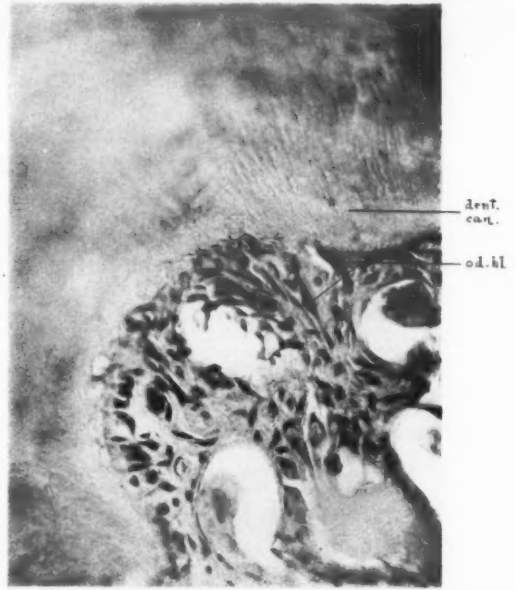


Fig. 20. Detail of Fig. 19.

dent can dental canal, *od bl* odontoblasts.

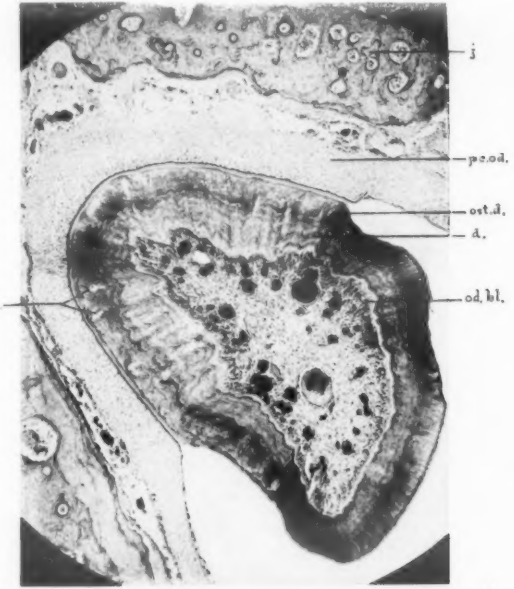


Fig. 21. Healing scurvy. No. 78.

Cross section of incisor, low power. In the dentin, wich is folded and irregular, bone canals *(Hav can)* are seen in the outer layer.

od bl irregular odontoblasts, *pe od* periodontium, *j* jaw bone, *ost d* osteodentin, *d* dentin.

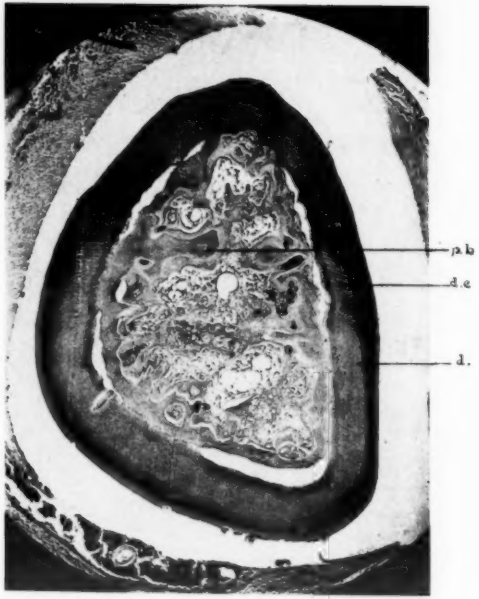


Fig. 22. Scorbut manifestus mitior, 0.1 m. pr. d. 42 days. No. 122.

Cross section of incisor, low power. Pulpa bone *(pb)* fills the pulp.

d old dentin with dilated *d e* Tomes' canals.

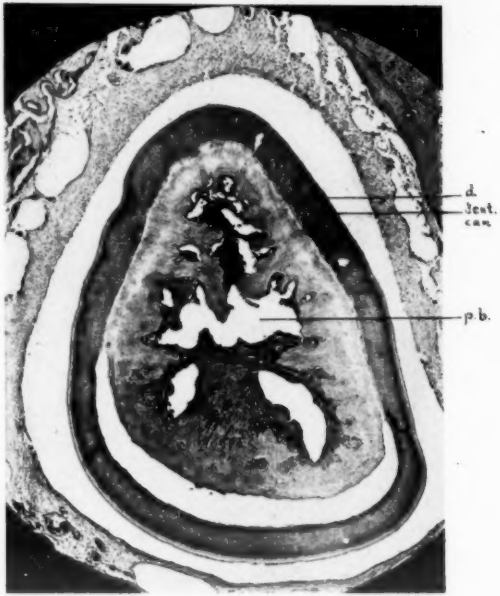


Fig. 23. Scorbut mitior latens extensus, 0.2 m. pr. d. 29 days. No. 130.

Cross section of incisor, low power. Pulpa bone *(pb)* fills the pulp.

d old dentin with dilated *d e* Tomes' canals.

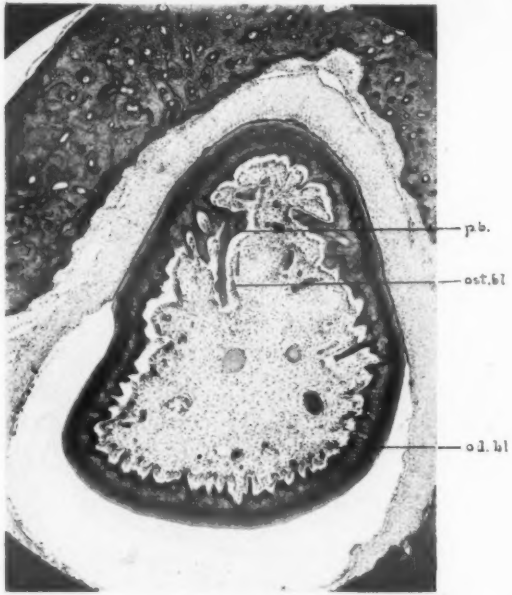


Fig. 24. Scorbut mitior latens extensus, 0.3 m. pr. d. 83 days. No. 135.

Cross section of incisor, low power.

pb pulpa bone, *o l bl* odontoblasts in disorder, *ost bl* osteoblasts.

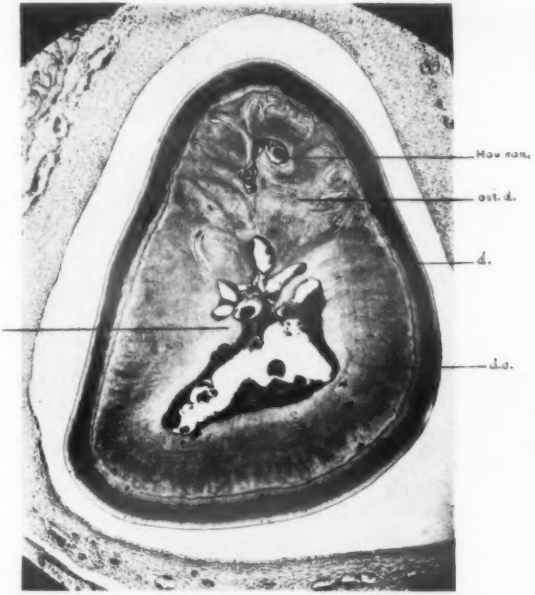


Fig. 25. Scorbut mitior latens levior, 0.5 m. pr. d. 92 days. No. 144.

ost d osteodentin, *pb* pulpa bone, *Hav can* bone canals, *d* dentin *d c* dental canals.

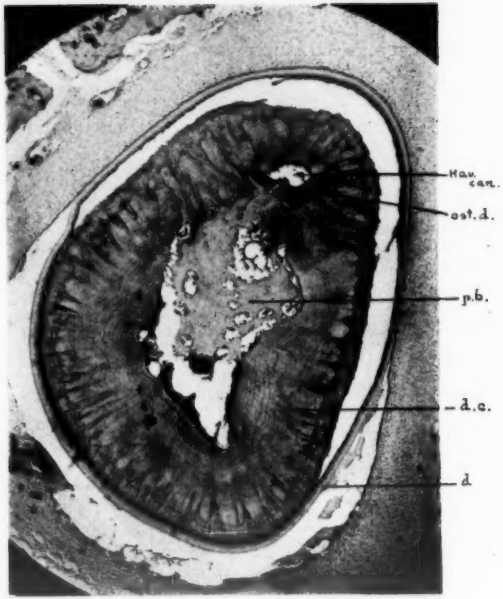


Fig. 26. Scorbut mitior latens levior, 0,7 m. pr. d. 22 days. No. 152.

Abbreviations = Fig. 25.

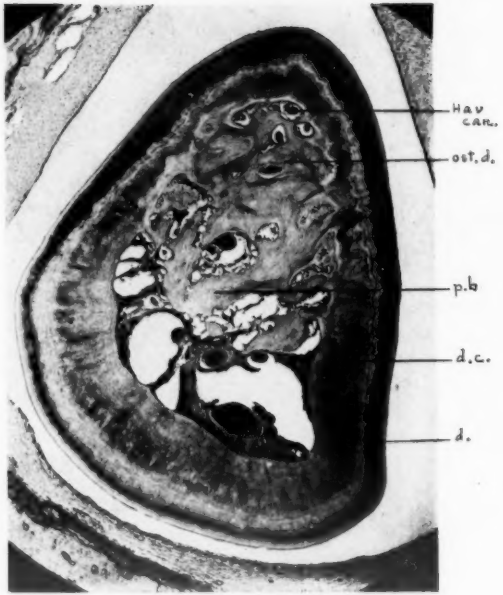


Fig. 27. Scorbut mitior latens levior, 0.7 m. pr. d. 92 days. No. 156.

Abbreviations = Fig. 25.

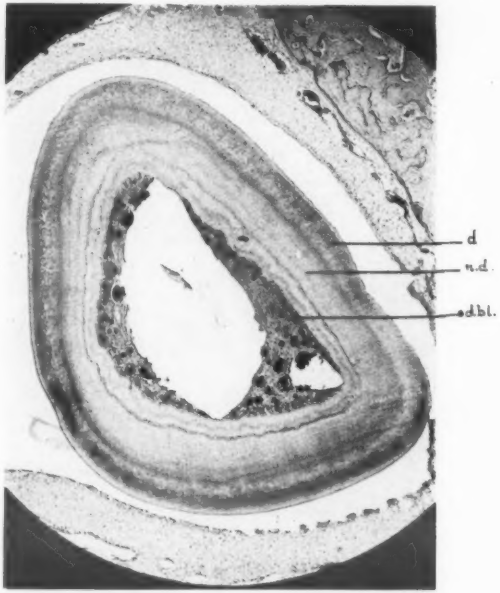


Fig. 28. Scorbut mitior latens levior, 0.8 m. pr. d. 29 days. No. 159.

Old dentin *(d)* without distinct changes. New dentin *(n d)* lighter, with irregular inner edge. *od bl* odontoblasts in disorder.

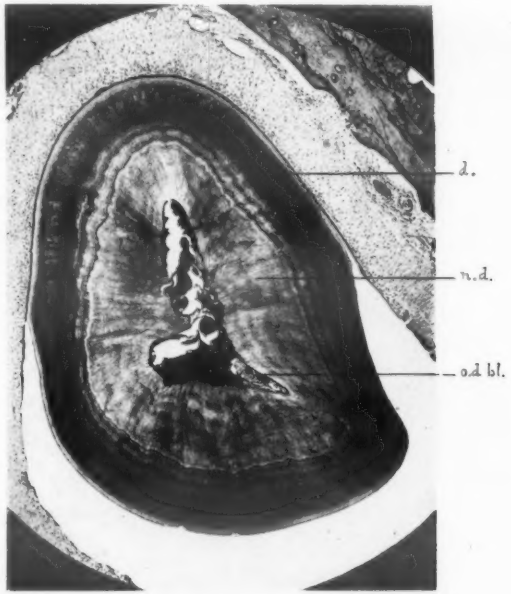


Fig. 29. Scorbut mitior latens levior, 0.8 m. pr. d. 92 days. No. 161.

Abbreviations = Fig. 28.

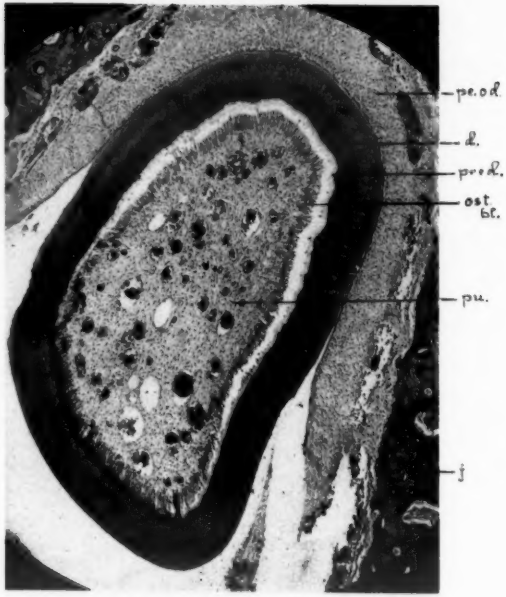


Fig. 30. No scurvy. > 1 m. pr. d. No. 176.
pe od periodontium, *d* dentin, *pred* predentin, *ost bl* osteoblasts, *pu* pulp, *j* jaw bone.

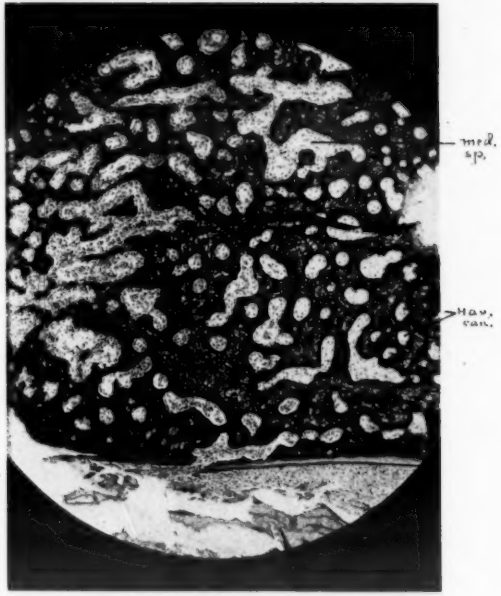


Fig. 31. Scorbut manifestus gravior, 38 days. No. 3.
Oblique cross section of molar. No free pulp, but in the medullary spaces *(med sp)* and bone

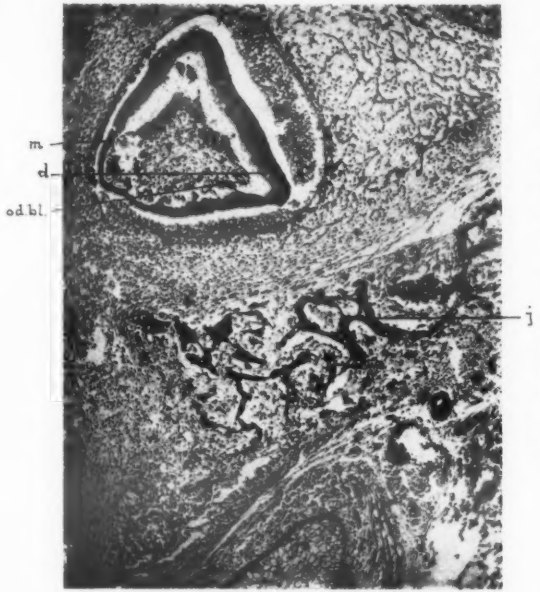


Fig. 32. No scurvy.
Section of embryonal jaw.
m molar, *j* jaw-bone, *d* dentin, *od bl* odontoblasts.

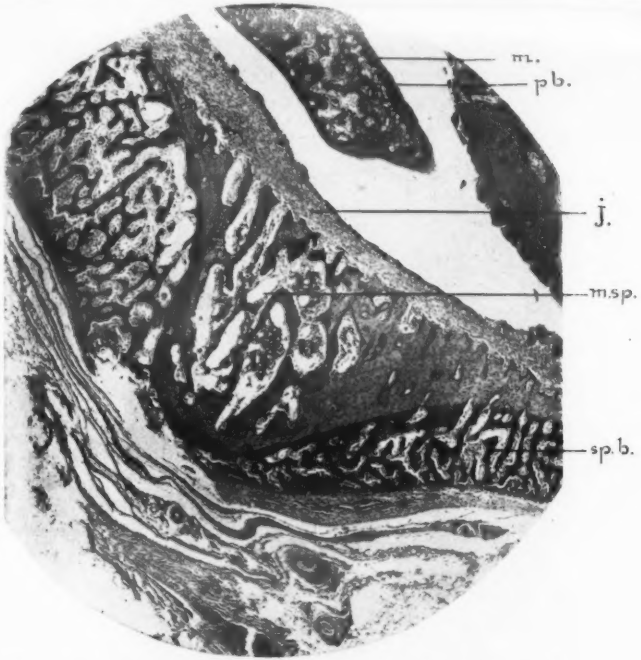


Fig. 33. Scorbut manifestus mitior, 0.2 m. pr. d. 42 days. No. 67.
Cross section of lower jaw, high power. Formation of spongy bone *(sp b)* outside the old jaw *(j)*, which shows osteoporosis.
med sp medullary spaces, dilated, *m* apex of molar with pulpa bone *(pb)*.

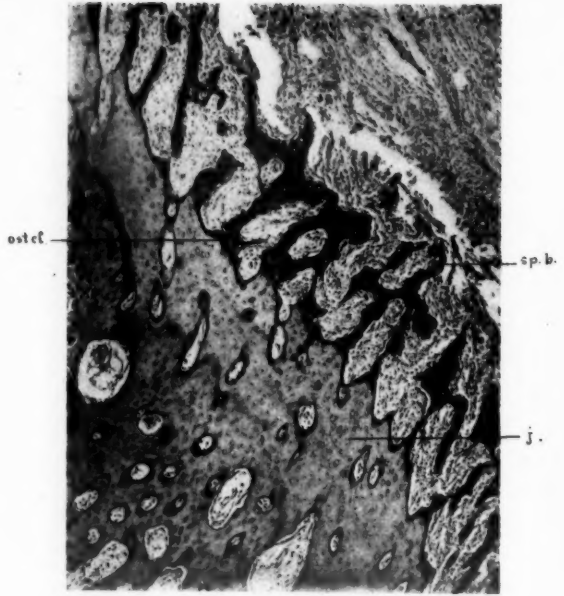


Fig. 34. Scorbut manifestus gravior, 24 days. No. 1.

Cross section of lower jaw, high power. Resorption of the new, spongy bone.

ost cl = osteoclasts.

Fig. 35. Scorbus mitior latens extensus, 0.3 m. pr. d. 43 days. No. 140.

Frontal section of rib. Periosteal bone of spongy character.

mu atrophied muscle, *c c* cartilage columns, low.

Fig. 36. No scurvy. No. 96.

Frontal section of rib. Normal picture.

c c cartilage columns, *b* bone, *ma* marrow, *c* cartilage, *pe* periosteum, *mu* muscles.

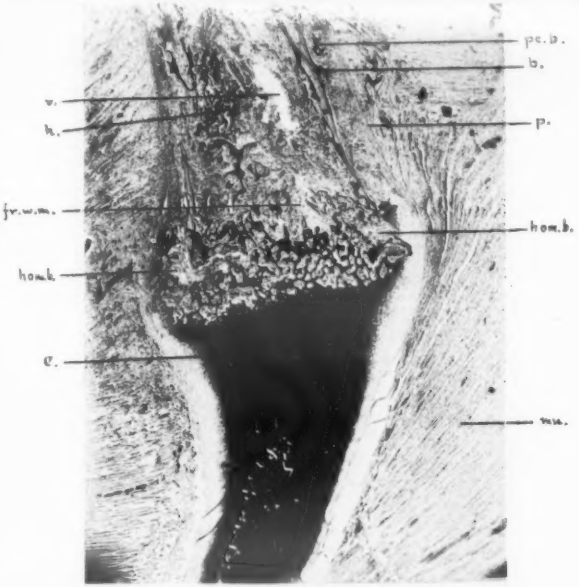


Fig. 37. Scorbut manifestus mitior, 0.1 m. pr. d. 59 days. No. 88.

Frontal section of rib, showing typical scorbutic changes in the enlarged costochondral junction.

c cartilage, *c c* cartilage columns in disorder, *calc c* primarily calcified cartilage, growing into the marrow, *hom b* homogeneous scorbutic bone, in the outer angle connected with cartilage and bone columns, *pe b* spongy periosteal bone, *fr w m* frame-work marrow, *v* dilated vein, *p* periosteum, *mu* atrophied muscle fibres, *b* old bone bridge, *h* hemorrhage.

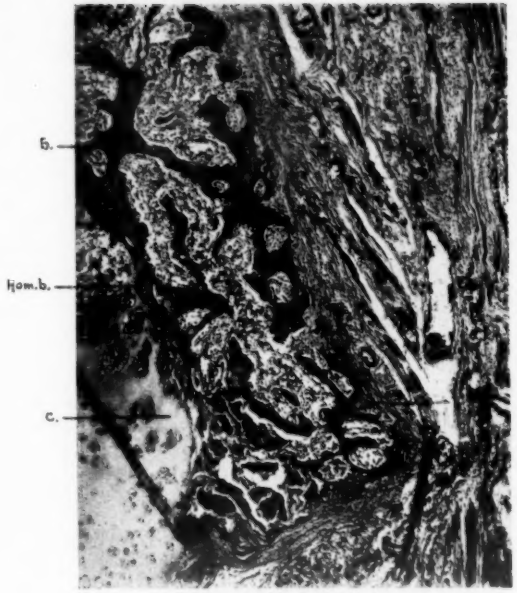


Fig. 38. Scorbut mitior latens extensus, 0.3 m. pr. d. 77 days. No. 139.

Frontal section of rib, one angle; high power. Inferior bone *(hom b)*, joins cartilage *(c)* and old bone *(b)*.

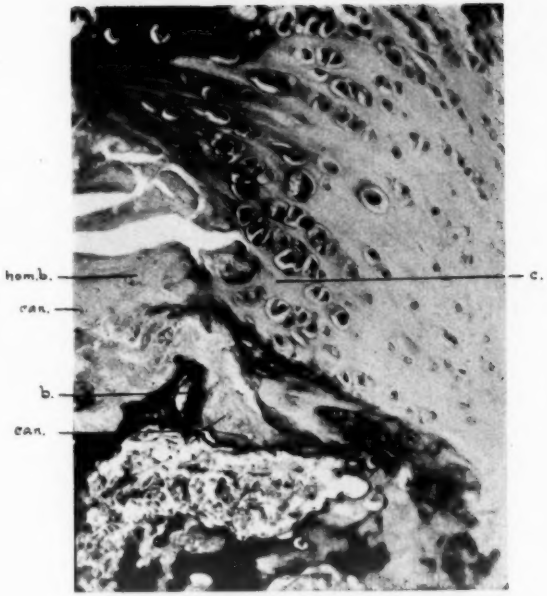


Fig. 39. Scorbut manifestus mitior, 0.1 m. pr. d. 59 days. No. 88.

Frontal section of rib, high power. In the homogeneous new bone *(hom b)* there are canaliculi *(can)*.

old bone (*b*).

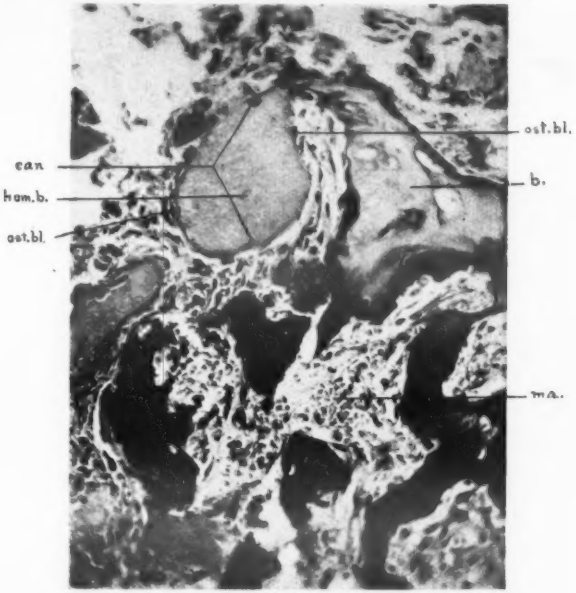


Fig. 40. Scorbut manifestus mitior, 0.1 m. pr. d. 59 days. No. 88.

Frontal section of rib, detail, high power.

ma bone marrow, deficient in cells, *b* bone bridges, *hom b* homogeneous new scorbutic bone, *can* canaliculi, *ost bl* osteoblasts, spool-shaped.

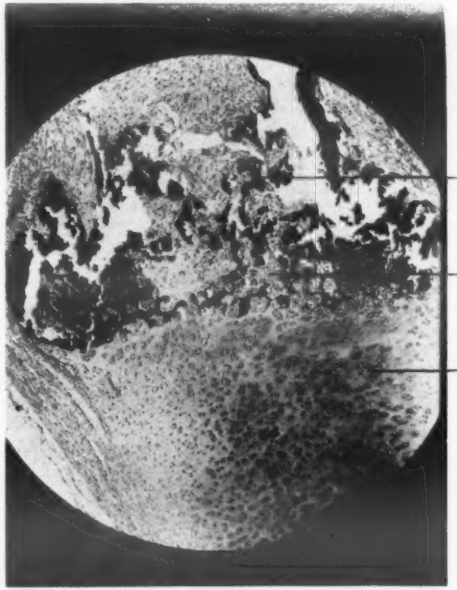


Fig. 41. Scorbut manifestus mitior, 0.1 m. pr. d. 50 days. No. 69.

Frontal section of rib, low power. Stained according to v. Kossa.

Calc b calcified cartilage and bone, *fr w m* frame-work marrow.

a

b

Fig. 42. Radiogram of the front chest wall of scorbutic *(a)* and normal *(b)* guinea-pig. a No 68, b No 189.

The dark shadow in the anterior epiphyses of the ribs in scurvy is clearly demonstrated.

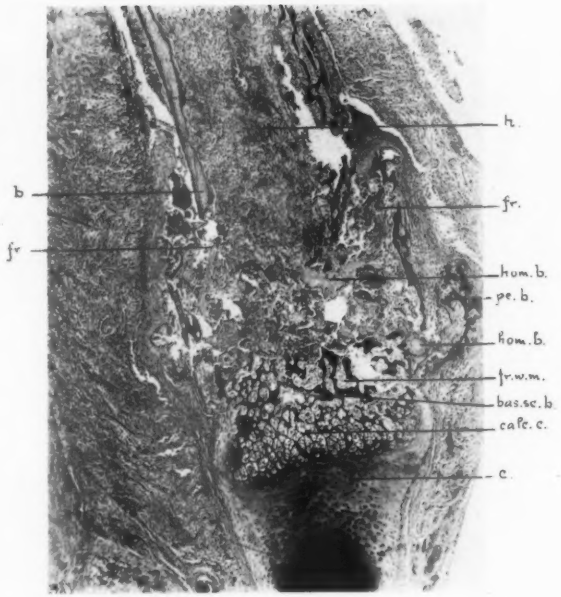


Fig. 43. Scorbut manifestus mitior, 0.1 m. pr. d. 59 days. No. 88.

Abundant formation of new scorbutic bone *(hom b)*.

b old bone, *c* cartilage, *calc c* primarily calcified cartilage, *bas sc b* basophile scorbutic bone, *pe b* periosteal bone, *fr* fracture, *fr w m* frame-work marrow, *h* hemorrhage.

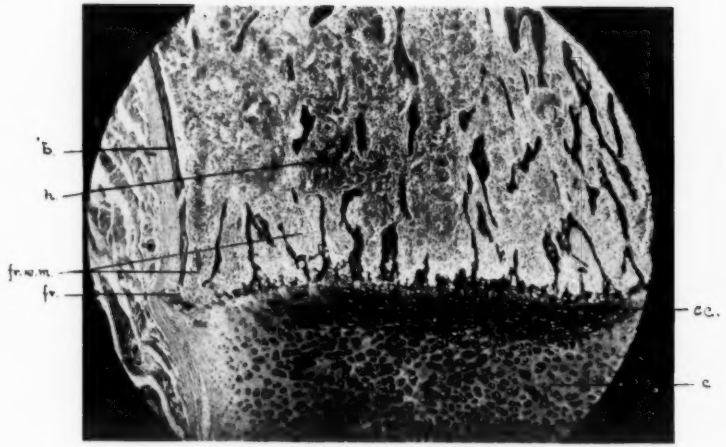


Fig. 44. Scorbut manifestus gravior, 24 days. No. 1.

Frontal section of rib, low power.

c cartilage, *c c* cartilage columns, low, *b* bone, *fr* fracture, *fr w m* frame-work marrow, *h* hemorrhage.

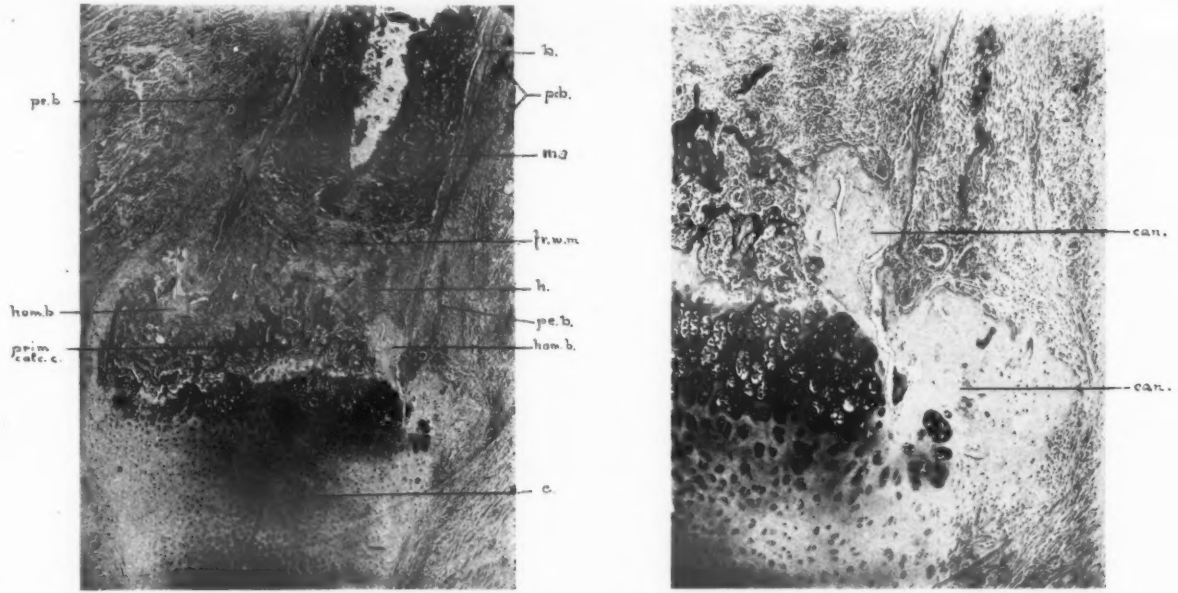


Fig. 45. Scorbut manifestus mitior, 46 days. No. 75.

a) Frontal section of rib, low power. b) Detail, high power. In the swollen costochondral junction there is an abundant formation of inferior bone in both angles.

hom b homogeneous scorbutic new bone, *can* canaliculi, numerous, *b* old bone, *prim calc c* primarily calcified cartilage, *c* cartilage, *fr w m* frame-work marrow, *pe b* periosteal spongy bone, *mj* hyperemic marrow, *h* hemorrhage.

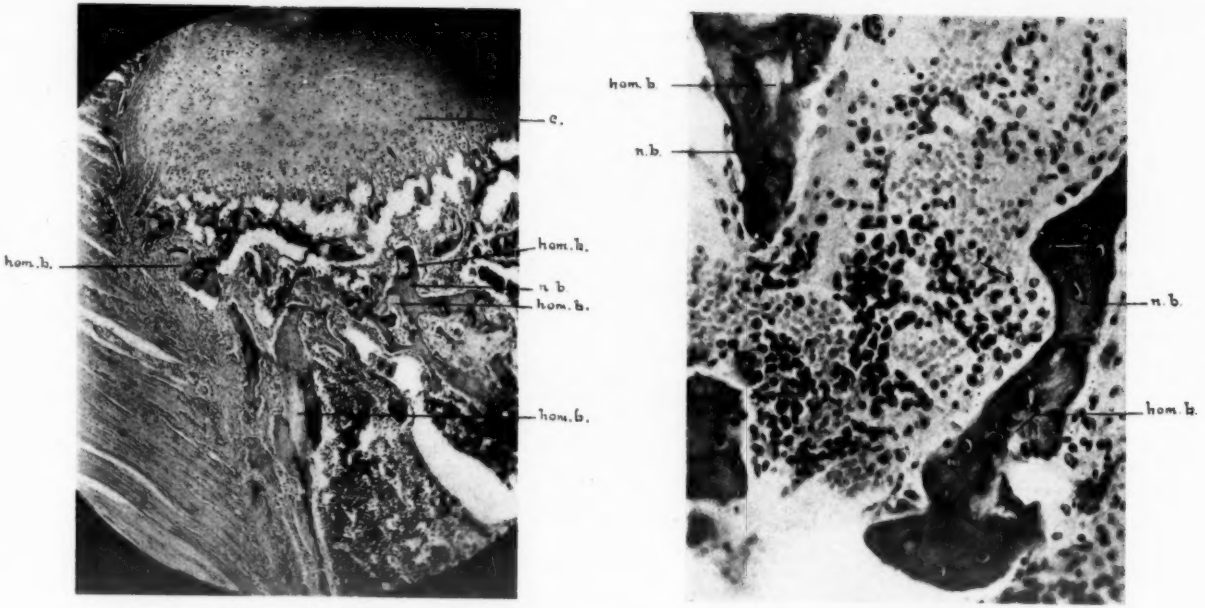


Fig. 46. Scurvy healing since 30 days.

Frontal section of rib. a) Low power, No. 76. b) High power No. 77. Remains of the homogeneous scorbutic bone *(hom b)* is seen in several places in the system of normal bone columns *(n b)*.

c cartilage.

c cartilage.

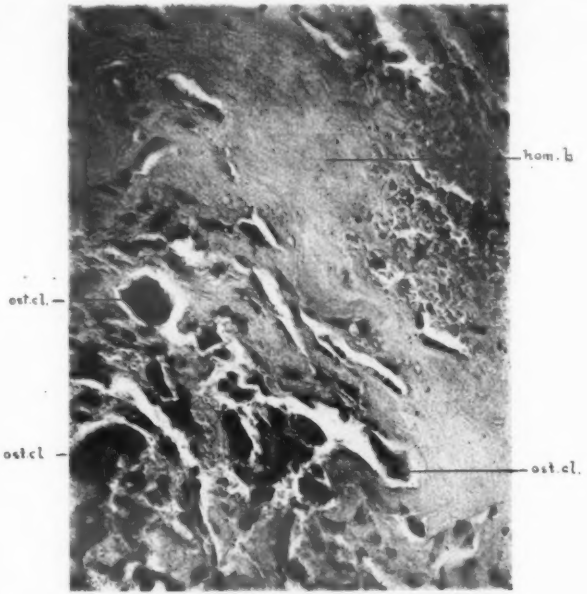


Fig. 47. Scorbut manifestus gravior, 24 days. No. 1.

Longitudinal section of the tibia, lower end; high power. Homogeneous new scorbutic bone *(hom b)* in resorption.

ost cl »osteoclasts«, syncytium of bone-cells.

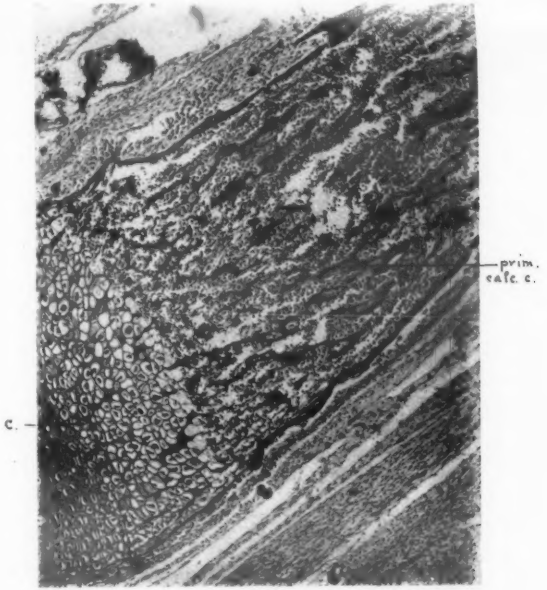


Fig. 48. Frontal section of rib, embryonal.

prim calc c primarily calcified cartilage.

Fig. 49 a. Infantile scurvy, Case 1.

Irregular pieces of bone *(i b)* are present in the system of more normal bone columns *(n b)*. Femur, lower epiphyseal end. High power.

Fig. 49 b. Infantile scurvy, Case 1.

In the angle between periosteum *(p)* and cartilage *(c)* there are numerous splinters of poorly developed bone *(sc b)*. Tibia, upper end. Low power.

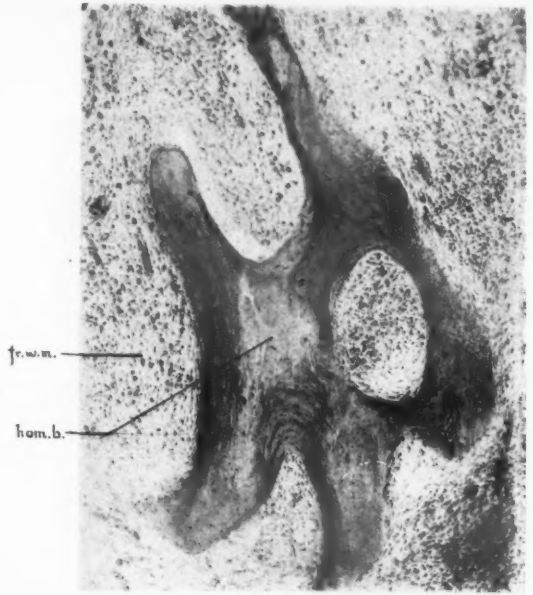


Fig. 49 c. Infantile scurvy, Case 1.
Homogeneous place *(hom b)* in otherwise more normal bone. Tibia, upper end. High power.

Fig. 50. Infantile scurvy. Case 3.
Femur, upper epiphysis. High power. Old bone columns *(n b)* through abundant homogeneous scorbutic bone *(hom b)* joined to cartilage *(c)*.

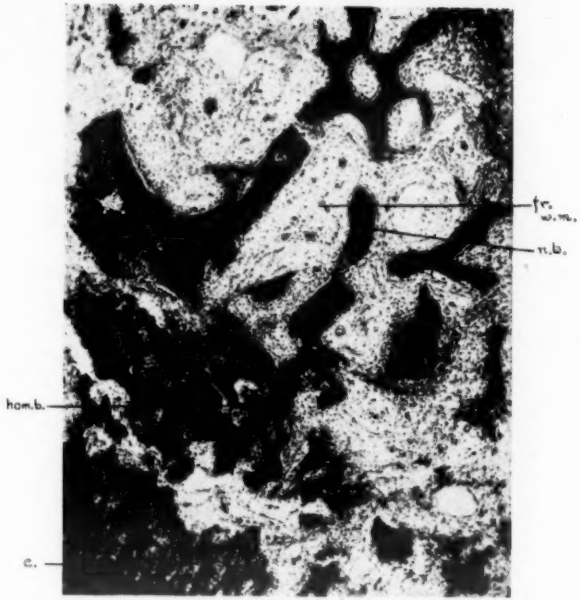


Fig. 51. Infantile scurvy. Case 4.

Rib, posterior end. Bone columns *(n b)*, lying in the frame-work marrow *(fr w m)*, joined to the cartilage *(c)* through a system of more homogeneous bone *(hom b)*.

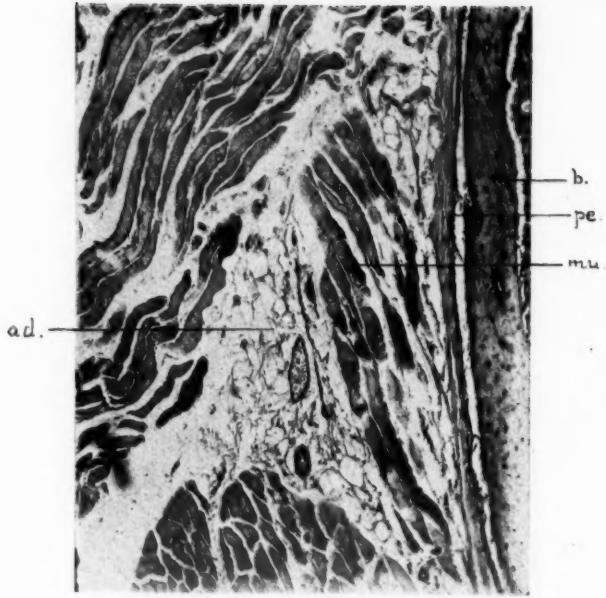


Fig. 52. No scurvy, 142 days.

Longitudinal section of rib interstice. Low power. Normal muscle.

Mu muscle fibre, *pe* periosteum, *b* bone, *ap* adipose tissue.

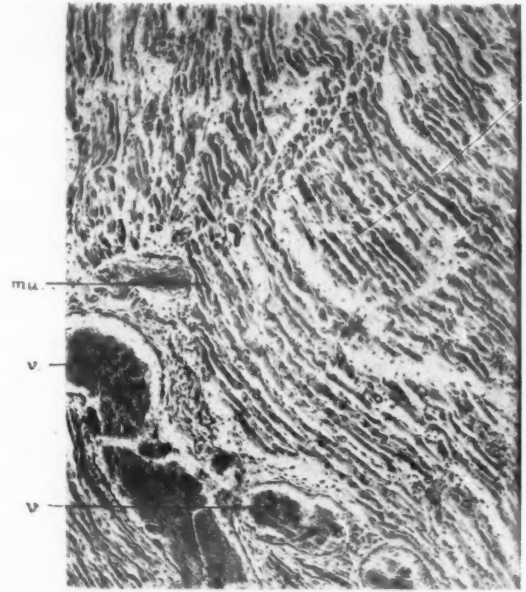


Fig. 53. Scorbut gravior manifestus, 32 days. No. 28.

Longitudinal section of rib interstice. Low power. Atrophy of the muscle fibres *(mu)*. Dilatation of the veins *(v)*.

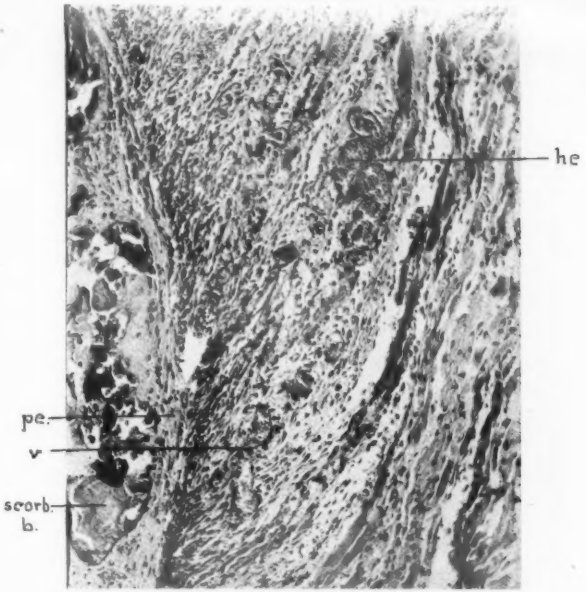


Fig. 54. Scorbut gravior manifestus, 26 days. No. 21.

Longitudinal section of rib interstice. Low power. The same muscular atrophy is seen all through as in the neighbourhood of the hemorrhages *(he)*.

v dilated vessels, *scorb b* new homogeneous scorbutic bone in the costal angle, *pe* periosteum.

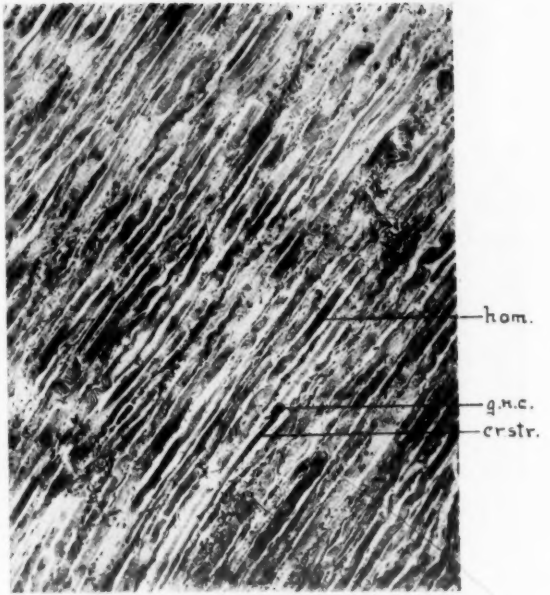


Fig. 55. Scorbut mitior manifestus, 0,1 m. pr. d. 59 days. No. 88.

Longitudinal section of rib interstice. Low power. Atrophy of muscle fibres, partly homogenized *(hom)*, partly with remaining cross-striation *(cr str)*.

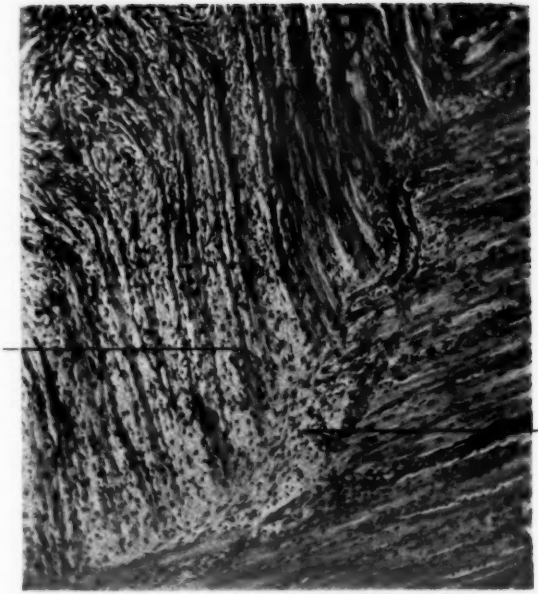


Fig. 56. Scorbut mitior manifestus, 0.1 m. pr. d. 60 days. No. 58.

Longitudinal section of rib interstice. Low power. Atrophy of the muscle fibres *(mu)*. Connective tissue *(c t)* increased.

partly with remaining cross-striation *(cr str)*.

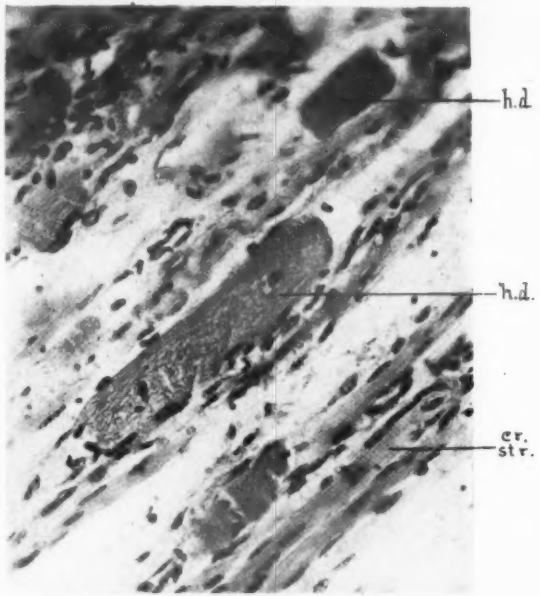


Fig. 57. Scorbut manifestus gravior, 38 days. No. 3.

Longitudinal section of rib interstice. High power. Atrophy of muscle fibres. Cross-striation *(cr str)* remaining in the fine fibres.

h d homogenized dot.

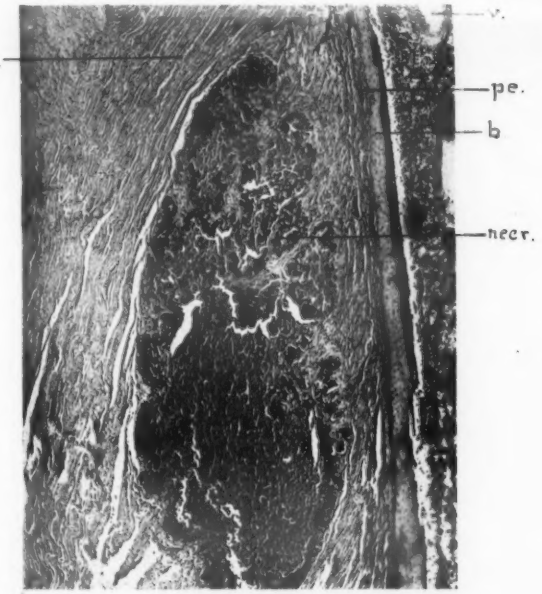


Fig. 58. Scorbut mitior manifestus, 0,2 m. pr. d. 60 days. No. 58.

Longitudinal section of rib interstice. Low power. Atrophic muscle *(mu)* with large calcified necrosis *(necr)*.

pe periosteum, *b* bone, *v* dilated vessels in the hyperemic marrow.

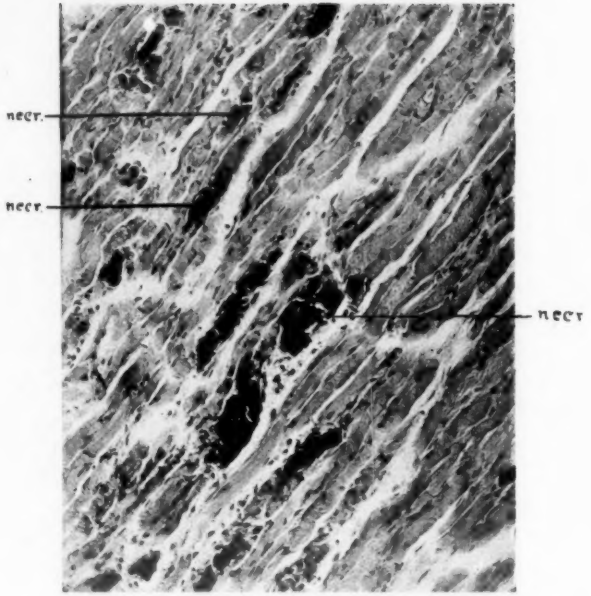


Fig. 59. Scorbut gravior manifestus, 22 days, No. 48.

Longitudinal section of rib interstice. High power. Calcified necrosis *(necr)* of musle fibres.

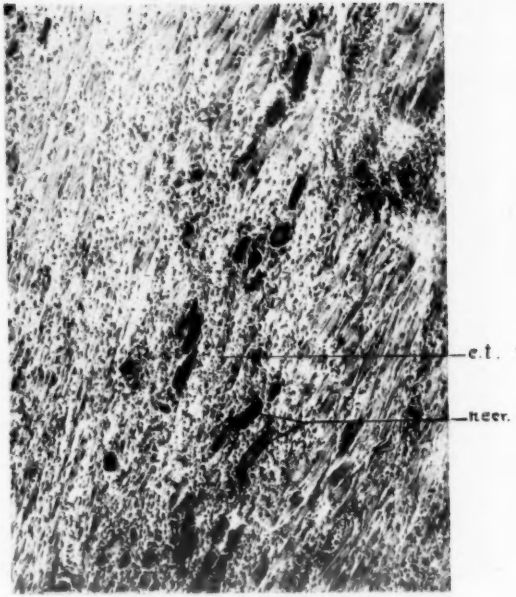


Fig. 60. Scorbut mitior latens extensus, 0,3 m. pr. d. 29 days. No. 63.

Longitudinal section of elbow. High power. Atro- and calcified necrosis *(necr)*.

Calcified necrosis *(necr)* of muscle fibres.

and calcified necrosis *(necr)*.

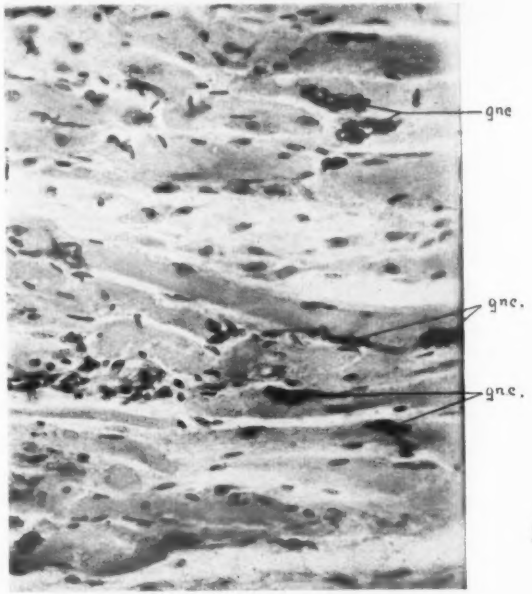


Fig 61. Scorbut mitior manifestus, 0,2 m. pr. d. 59 days. No. 88.

Longitudinal section of rib interstice. Very high power. Giant-nuclei cells *(gn)* in atrophic muscle.

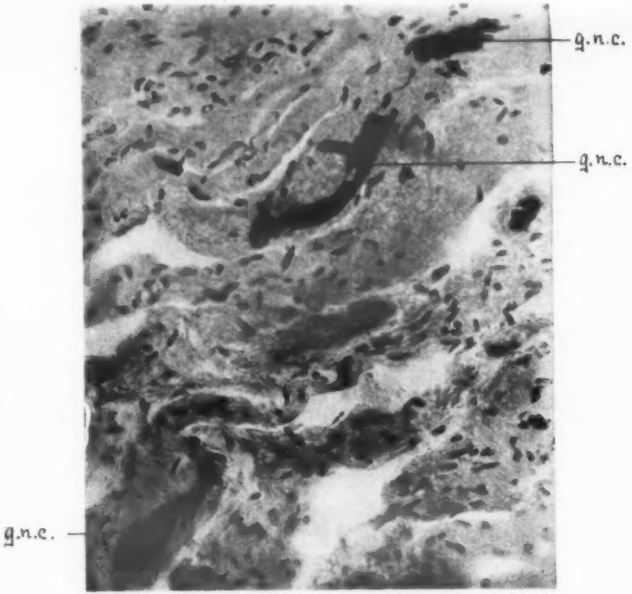


Fig. 62. Scorbut manifestus gravior, 35 days. No. 35

Longitudinal section of rib interstice. Very high power. Giant-nuclei cells *(gn)* in atrophic muscle.

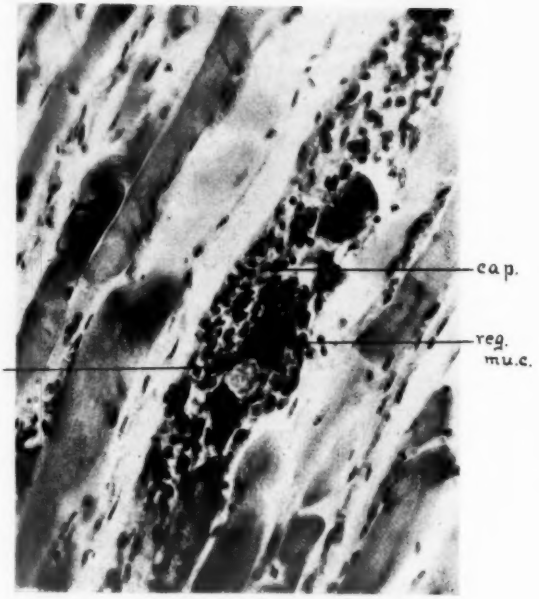


Fig. 63. Healing scurvy. No. 77.

Longitudinal section of rib interstice. Very high power. Regeneration of muscle.

c t connective tissue, *cap* capillaries, *reg mu c* giant syncytial muscle cell of regenerative type.

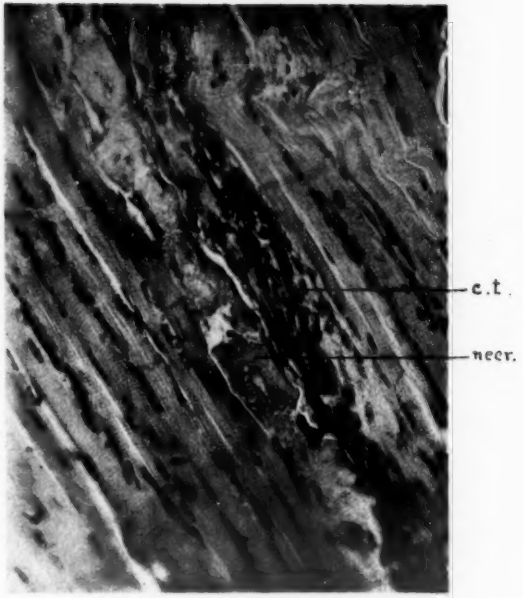


Fig. 64. Healing scurvy. No. 77.

Longitudinal section of knee. Very high power. Rest of necrotic fibres *(necr)* remaining. Connective tissue *(c t)* increased.

muscle cell of regenerative type.

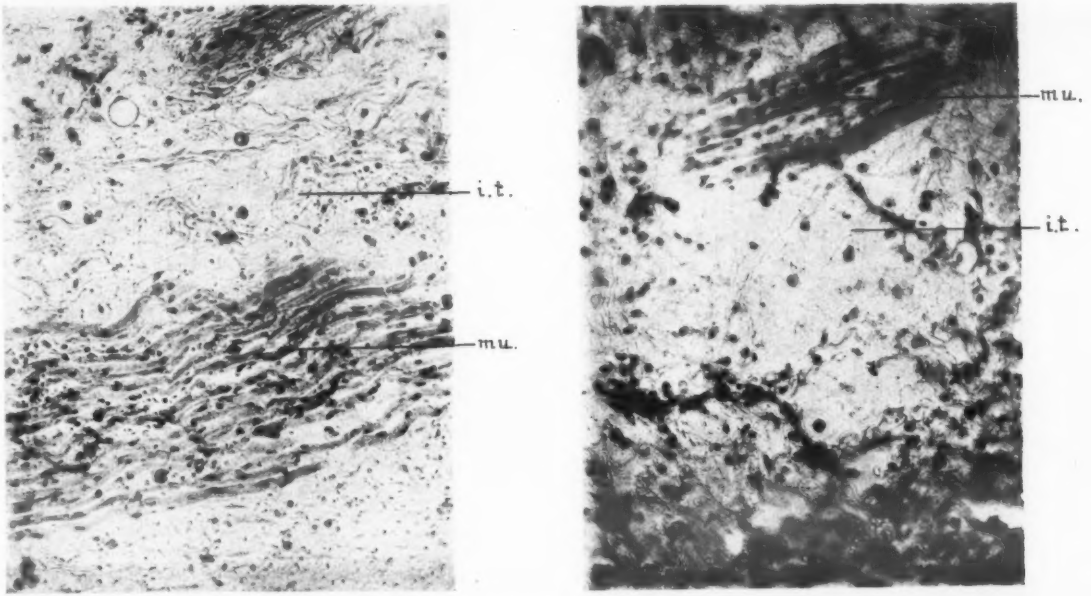


Fig. 65, a and b. Infantile scurvy. Case 3.

Longitudinal section of thigh. High power. Atrophy of muscle fibres *(mu)*. The interstitial tissue *(i t)* looks edematous.

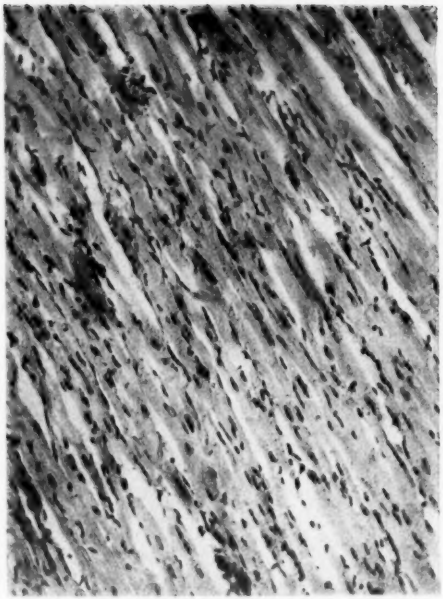


Fig. 66. Scorbut mitior latens levior, 0,8 m. pr. d. 92 days. No. 161.

Longitudinal section of heart. The musculature looks normal.

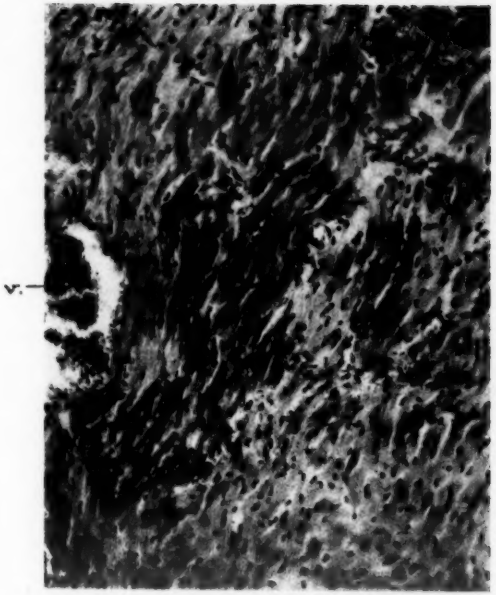


Fig. 67. Scorbut gravior manifestus, 19 days. No. 113.

Longitudinal section, heart. Muscle fibres homogenized, thickened, stained deeply by eosin.

v dilated vessels.

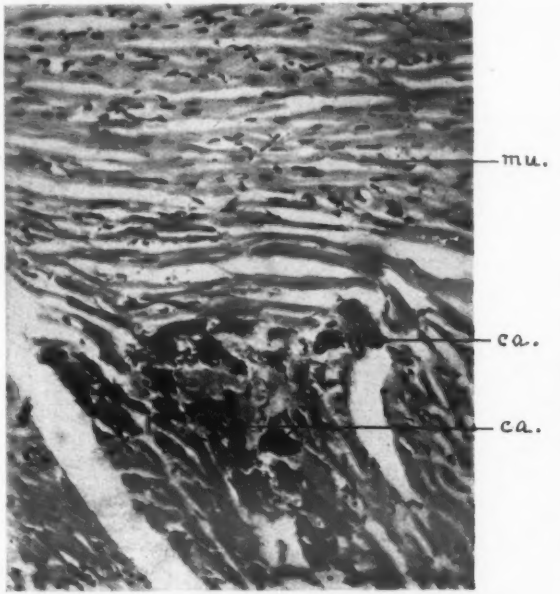


Fig. 68. Scorbut mitior manifestus, 0,5 m. pr. d. 18 days. No. 145.

Longitudinal section of heart. Low power. Calcium pigment *(ca)* in the fine, atrophic muscle fibres *(mu)*.

Fig. 69 Detail of Fig. 68. Very high power.

Calcium pigment deposed so as to make the cross-striation structure manifest.

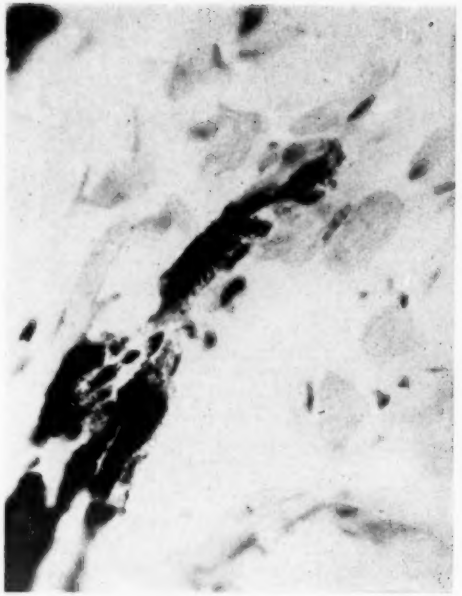


Fig. 70. Scorbut mitior manifestus, 0,2 m. pr. d. 43 days. No. 132.

Longitudinal section of heart. Very high power. The calcium pigment in the atrophic muscle fibres deposed so as to make the cross-striation structure manifest.

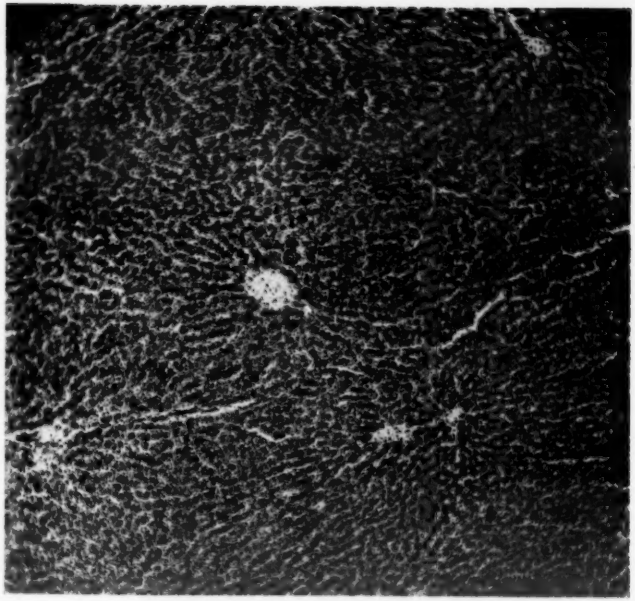


Fig. 71 No scurvy. No. 1.

Liver. Normal picture. Low power.

manifest.

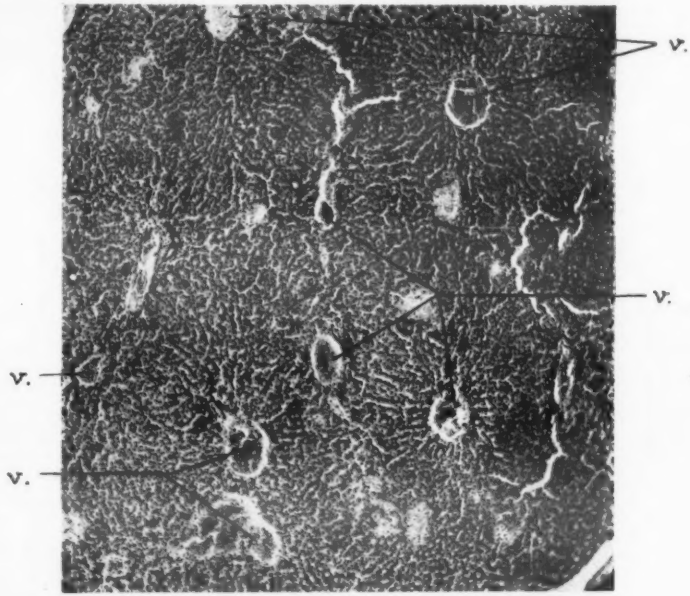


Fig. 72. Scorbut gravior manifestus, 37 days. No. 41.
Liver. Low power. Atrophy.
v central vein.

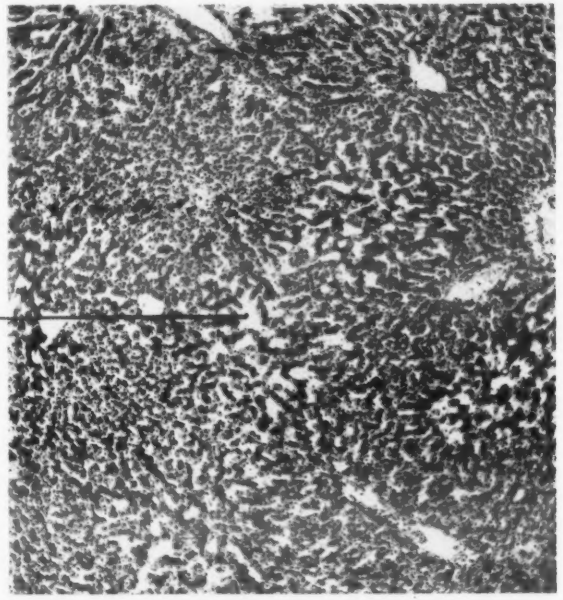


Fig. 73. Scorbut gravior manifestus, 35 days. No. 35.
Liver. Low power. Atrophy.
li co thin liver columns.

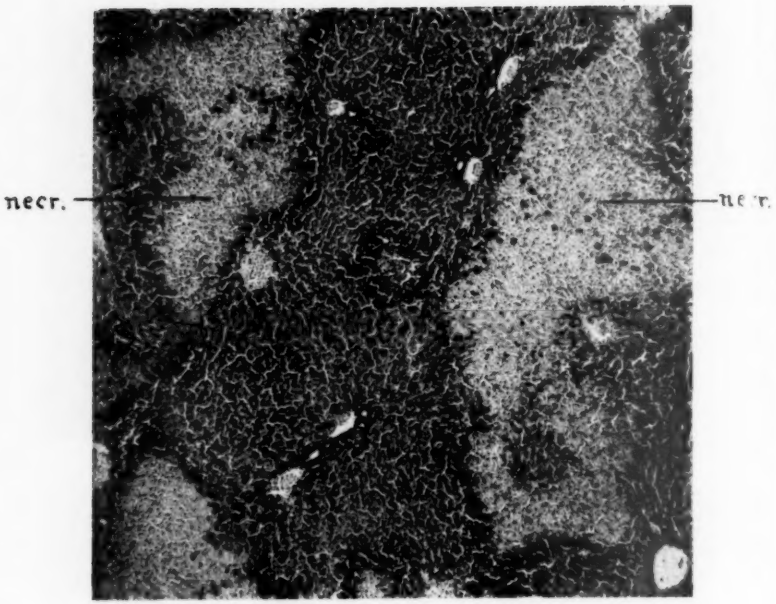


Fig. 74. Scorbut gravior manifestus, 30 days. No. 45.
Liver. Low power. Large necroses *(necr)*.

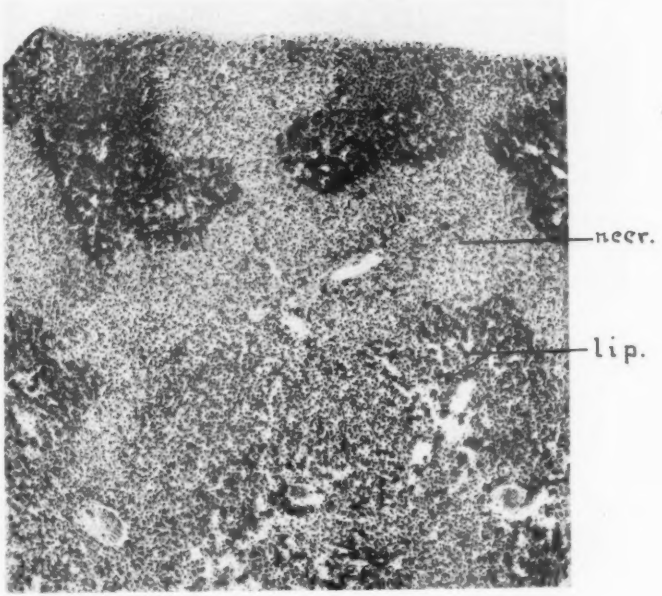


Fig. 75 Scorbut mitior manifestus, 0,2 m. pr. d. 39 days. No. 84.

Liver, sudan. Low power. Large necroses *(necr)* with small fat drops diffusely, larger *(lip)* at the edge.

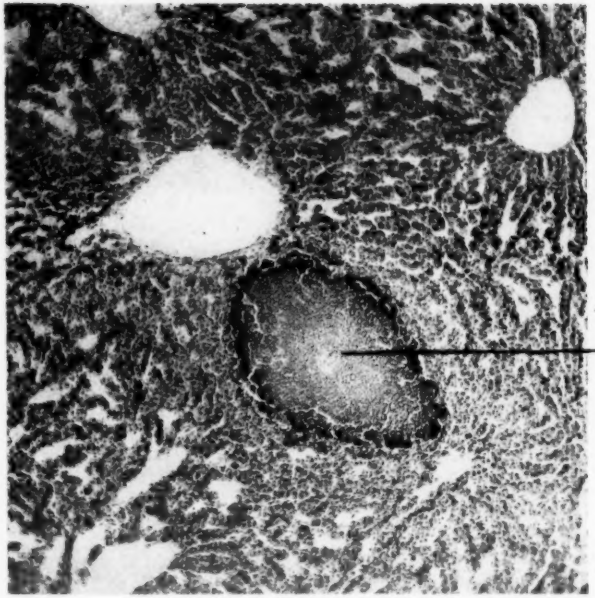


Fig. 76. Scorbut mitior manifestus, 0,2 m. pr. d., 43 days. No. 86.

Liver. Low power. Calcified necrosis *(necr)* with fibroblasts in the periphery.

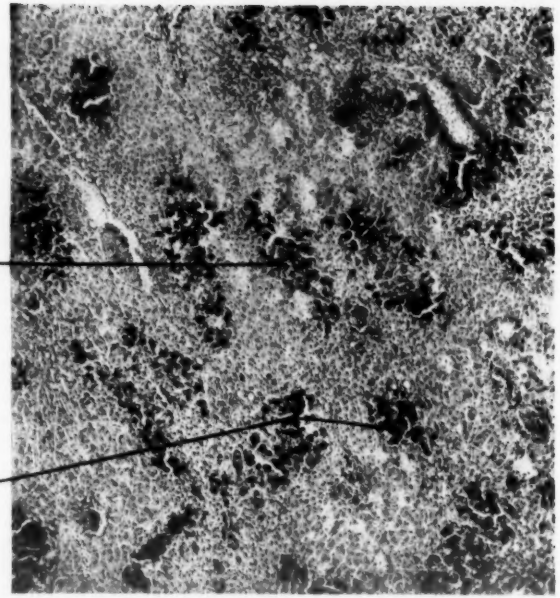


Fig. 77. Scorbut gravior manifestus, 28 days. No. 73.

Liver. Low power. Large irregular necroses, some with bilious pigment *(liv pigm)*, others calcified *(ca)*

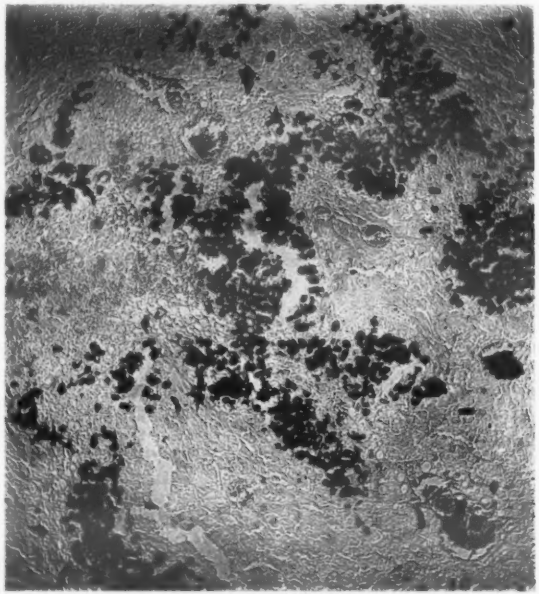


Fig. 78. Scorbut mitior manifestus. 0,2 m. pr. d. 43 days. No. 86.
Liver stained according to v. Kossa. Low power. Large necroses, surrounded by calcified grains.

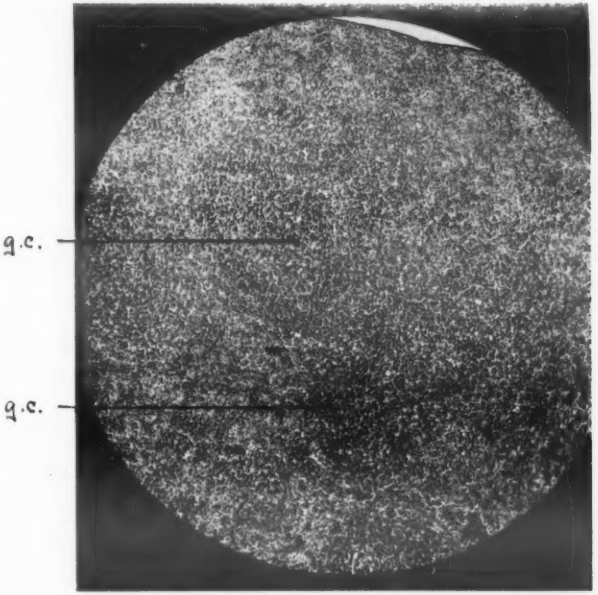


Fig. 79. No Scurvy. No. 11.
Spleen. Low power. Normal picture.
g c Malpighian corpuscle.

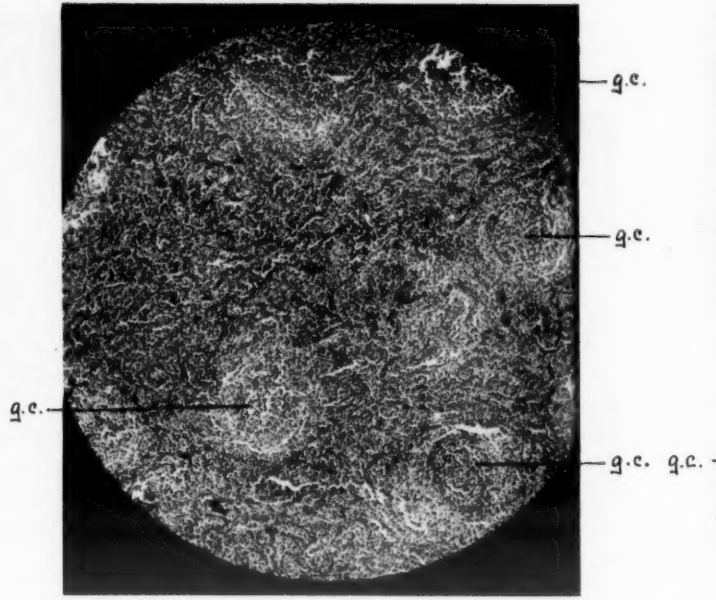


Fig. 80. Scorbut gravior manifestus, 37 days. No. 41.

Spleen. Low power. Atrophy of the lymphoid tissue, especially in the Malpighian corpuscles *(g c)*.

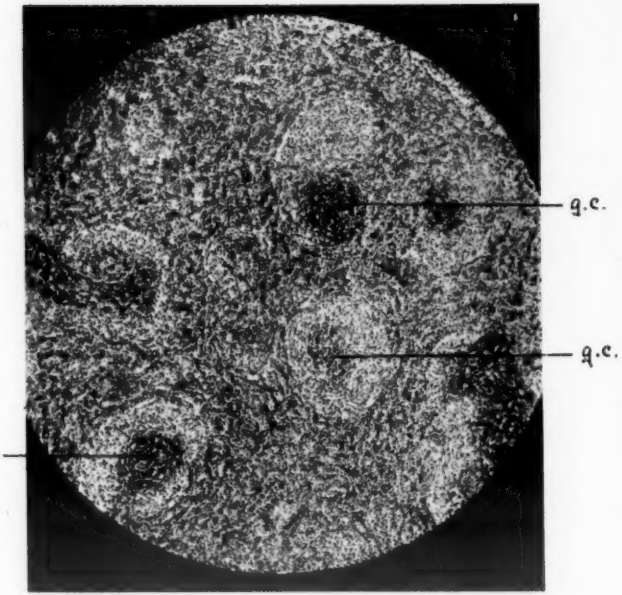


Fig. 81. Scorbut mitior manifestus, 0,3 m. pr. d. 60 days. No. 58.

Spleen. Low power. Atrophy of the lymphoid tissue, especially in the periphery of the Malpighian corpuscles *(g c)*.

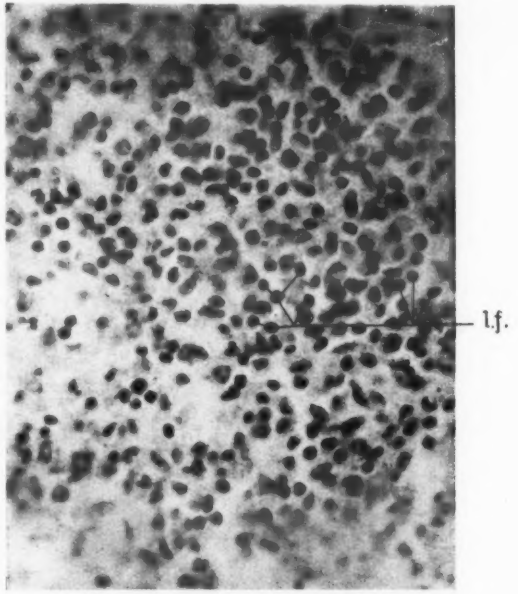


Fig. 82. No scurvy. No. 11.
Spleen. High power. Normal picture of pulp. Lymphocytes *(lf)* numerous.

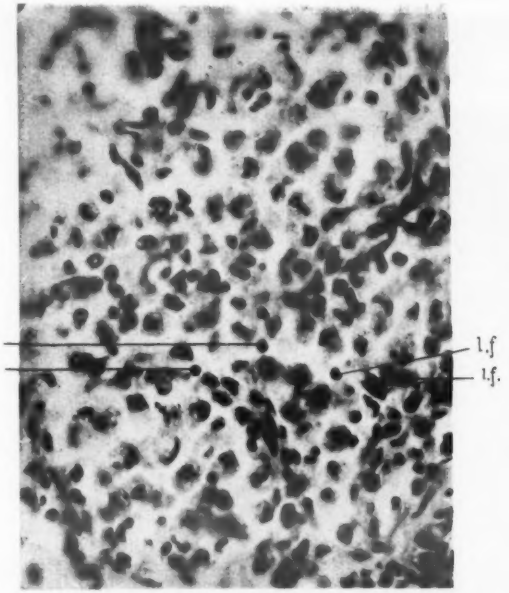


Fig. 83. Scorbut gravior manifestus, 37 days. No. 41.
Spleen. High power. Atrophy of the lymphoid tissue. The lymphocytes *(lf)* very sparse.

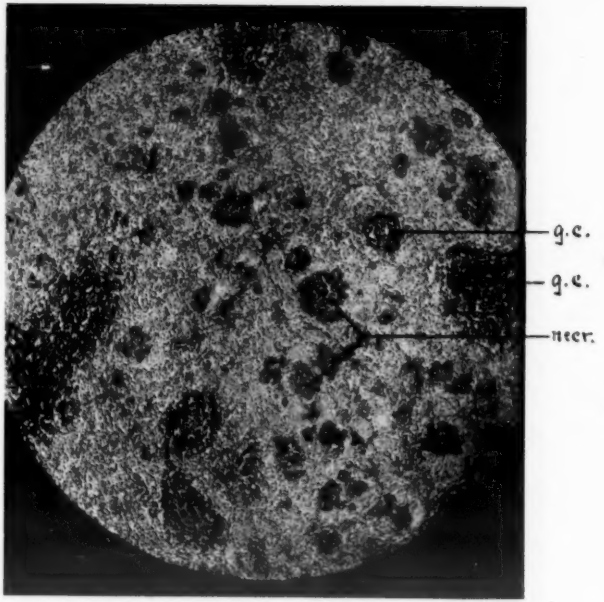


Fig. 84. Scorbut mitior manifestus, 0,1 m. pr. d. 15 days. No. 120.

Spleen, infection. Low power. Lymphocytic reaction weak. Numerous necroses *(necr)*.

g c Malpighian corpuscles.

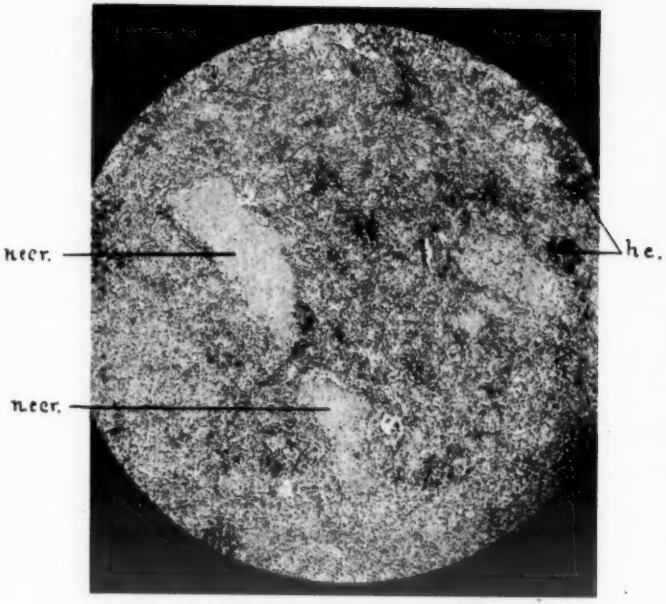


Fig. 85. Scorbut mitior latens extensus, 0,3 m. pr. d. 40 days. No. 138.

Spleen, infection. Low power. Weak lymphocytic reaction. Large necroses *(necr)* and hemorrhages *(he)*.

g c Malpighian corpuscles.

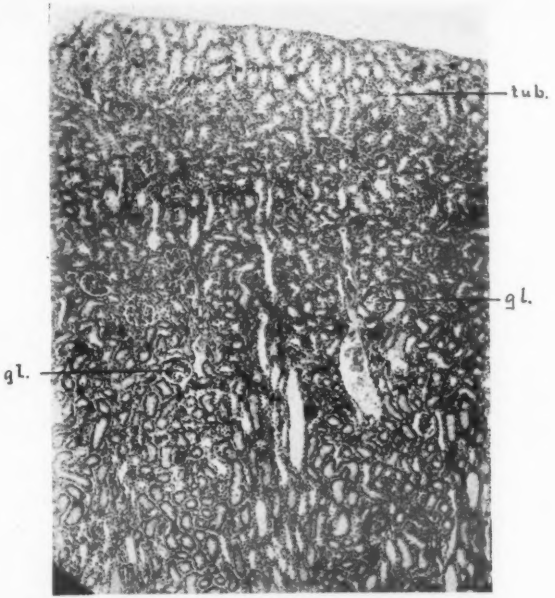


Fig. 86. No scurvy. No. 168.
Kidney, cortex. Low power. Normal picture.
gl glomeruli, *tub* tubules.

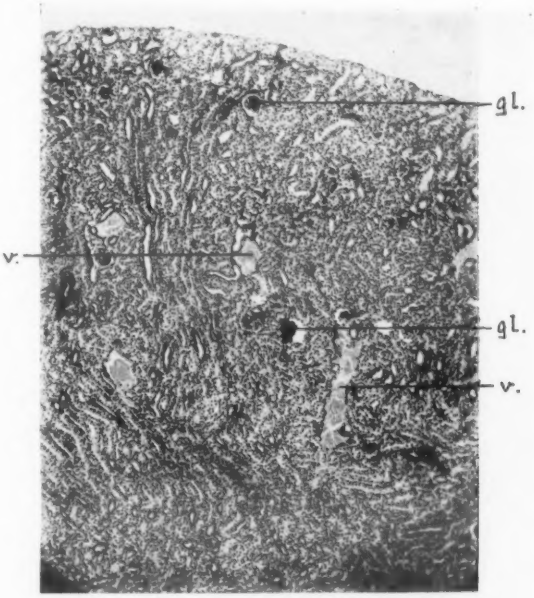


Fig. 87. Scorbut gravior manifestus, 19 days. No. 113.
Kidney, cortex. Low power. Atrophy with shrunk glomeruli *(gl)*.
v dilated vessels.

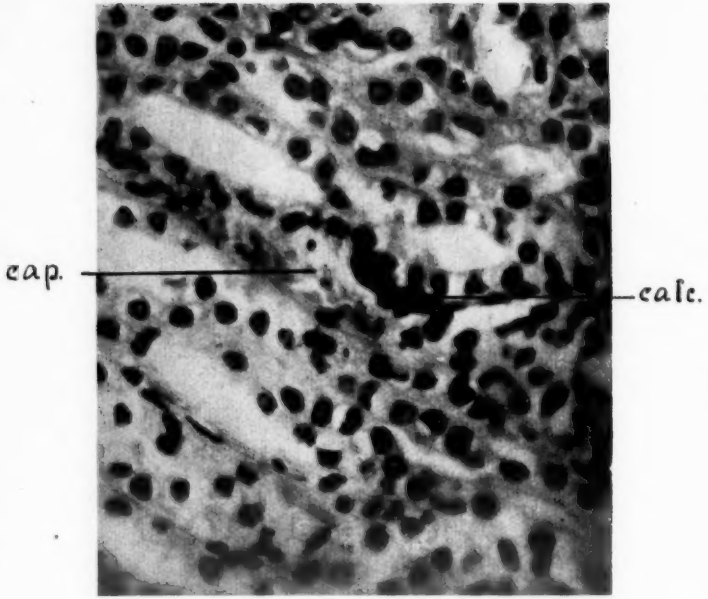


Fig. 88 a. Scorbut mitior latens extensus, 0.3 m. pr. d. 76 days. No. 142.

Kidney, marrow. High power. Calcium concretion *(calc)*. *calc* calcium between the nucleus and capillary *(cap)* of the epithelium cells.

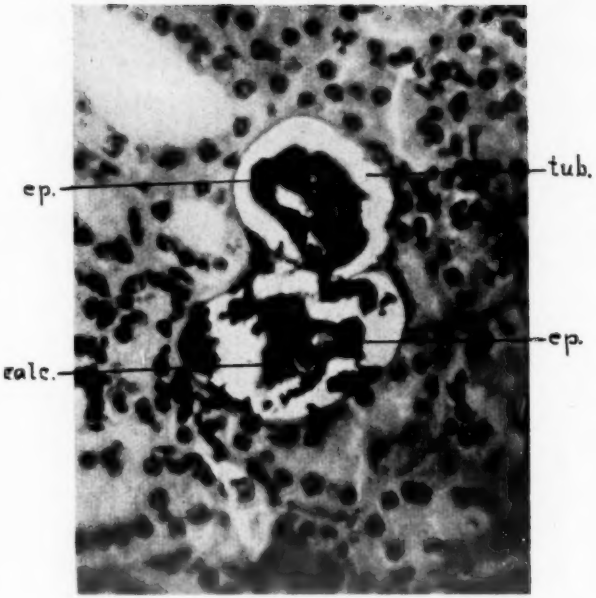


Fig. 88 b. Scorbut mitior latens extensus, 0.3 m. pr. d. 76 days. No. 142.

tub calcified tubules, *ep* epithelium cells.

calc. calcium between the nucleus and capillary (*cap*) of the epithelium cells.

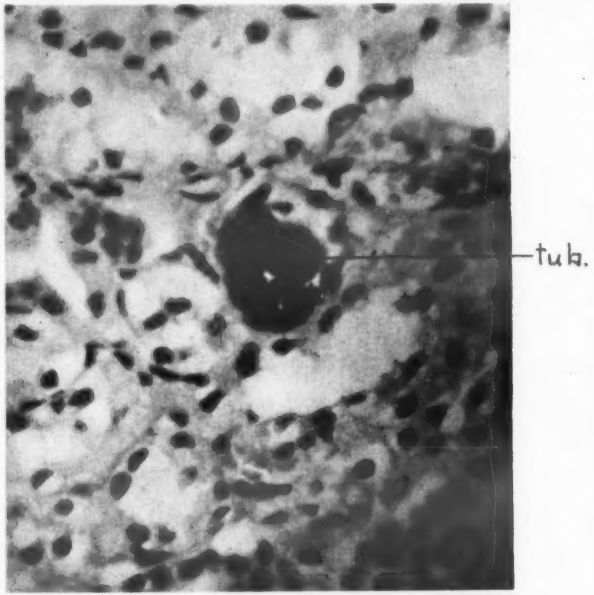


Fig. 88 c. Scorbut mitior latens extensus, 0.3 m. pr. d. 76 days. No. 142.
tub calcified tubule.

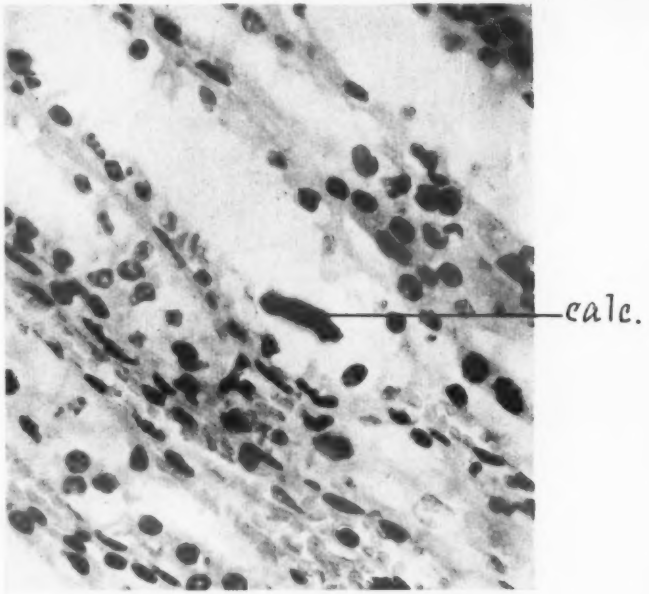
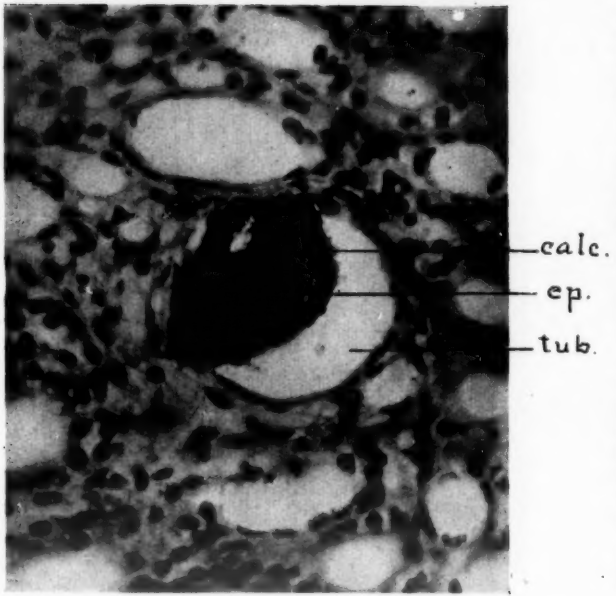


Fig. 88 d. Scorbut mitior latens extensus, 0.3 m. pr. d. 76 days. No. 142.
calc calcium concretion in the lumen of a tubule.

a



b

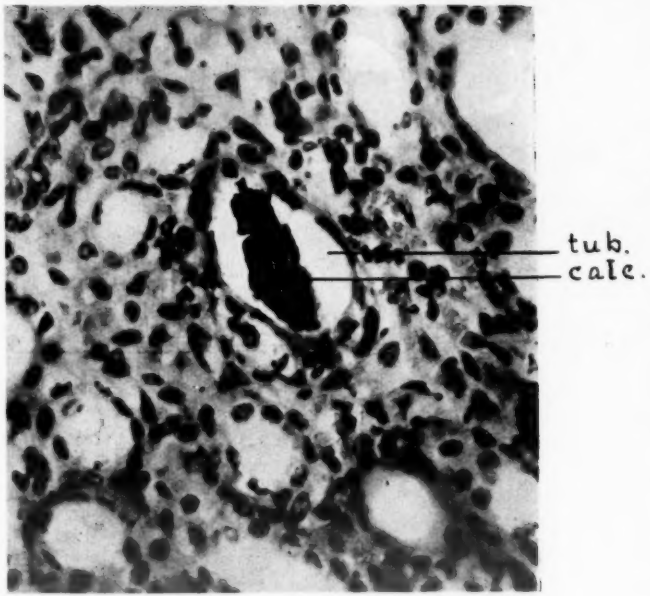


Fig. 89. Scorbut mitior latens levior, 0.8 m. pr. d., 82 days. No. 161.
Kidney, marrow. High power.

a) *calc* calcium concretion, subepithelially, bulging the epithelium [illegible] bule *(tub)*. b) *calc* calcium concretion in the free lumen of a tubule *(tub)*.

bule *(tub)*. b) *calc* calcium concretion in the free lumen of a tubule *(tub)*.

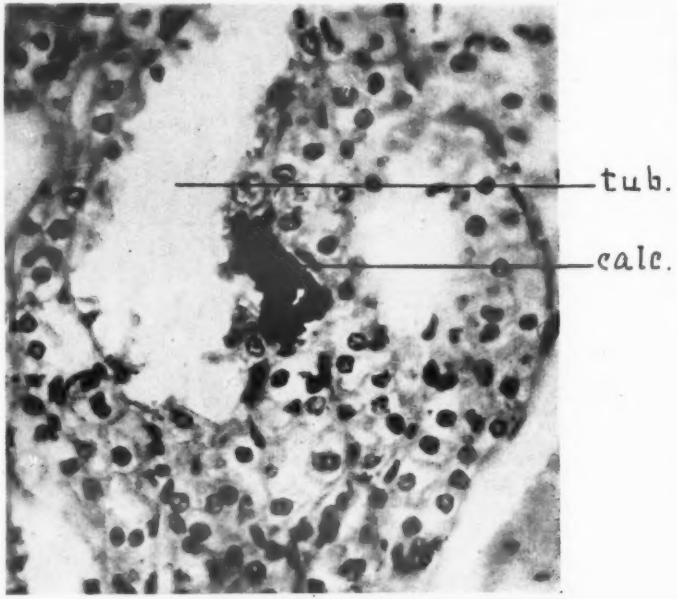


Fig. 90. Scorbut mitior latens extensus, 0.3 m. pr. d., 83 days. No. 135.
Kidney, marrow. High power.
calc calcium concretion in the wall of a tubule *(tub)*.

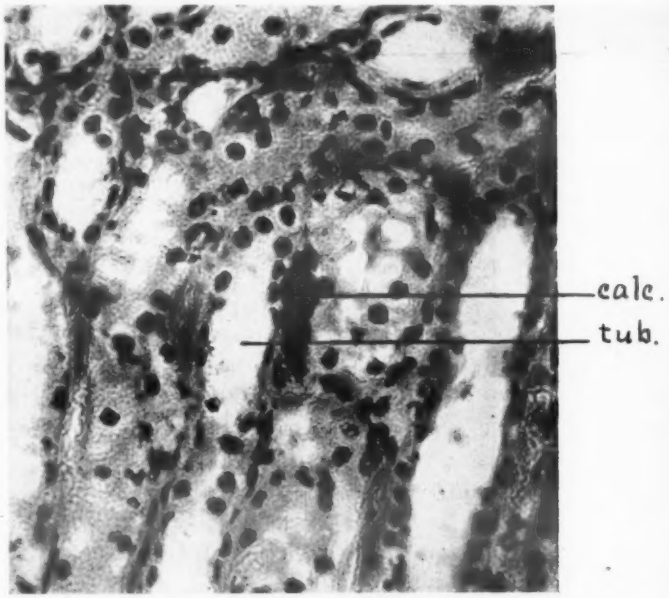


Fig. 91 a. Convalescence of beriberi. No. 83.
Kidney, marrow. High power.
calc calcium concretion subepithelially, *tub* tubule.

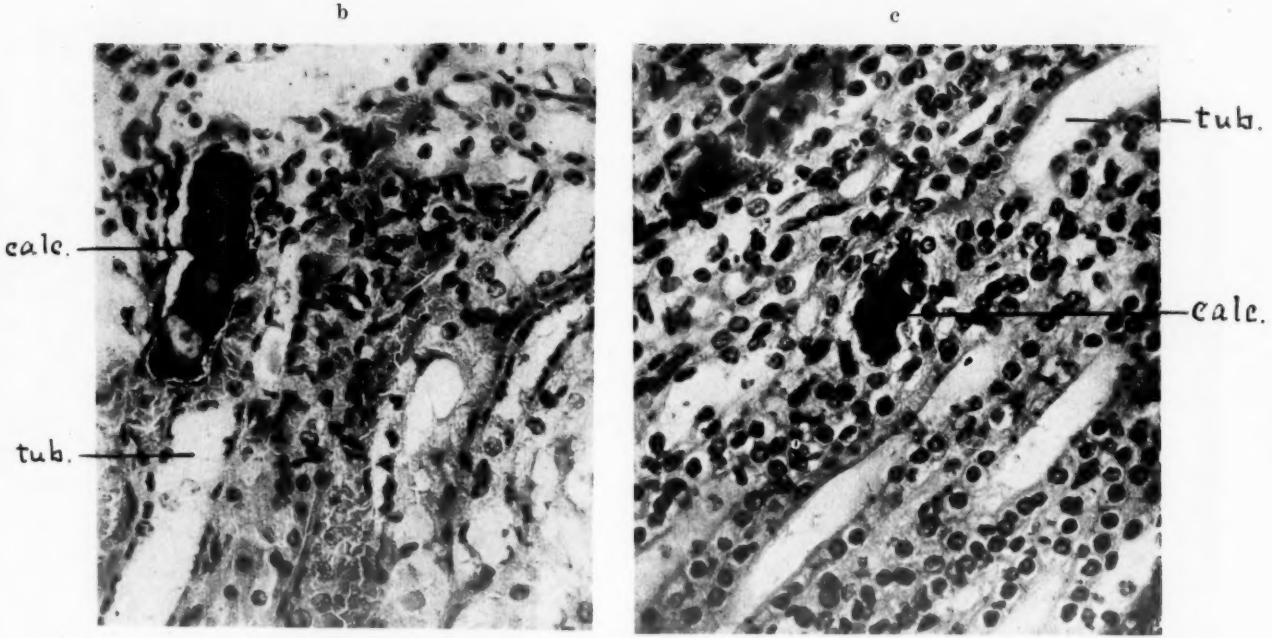


Fig. 91 b, c.

calc calcium concretion in the lumen of a tubule *(tub.)*.

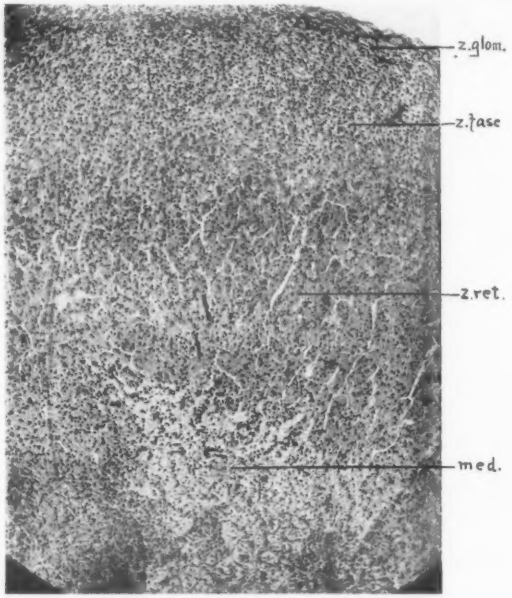


Fig. 92. No scurvy. No. 178.

Adrenal. Low power. Normal picture.

z glom zona glomerulosa, *z fasc* zona fasciculata, *z ret* zona reticularis *med* medulla.

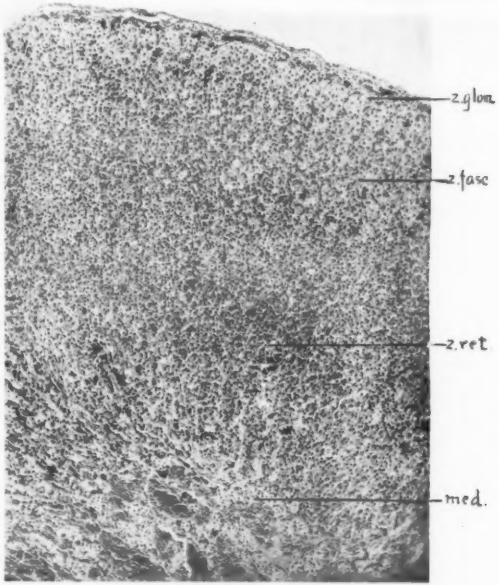


Fig. 93. Scorbut mitior manifestus, 0.1 m. pr. d., 25 days. No. 121.

Adrenal. Low power. Atrophy, hyperemia.

z glom zona glomerulosa, *z fasc* zona fasciculata, *z ret* zona reticularis, *v* dilated vessel.

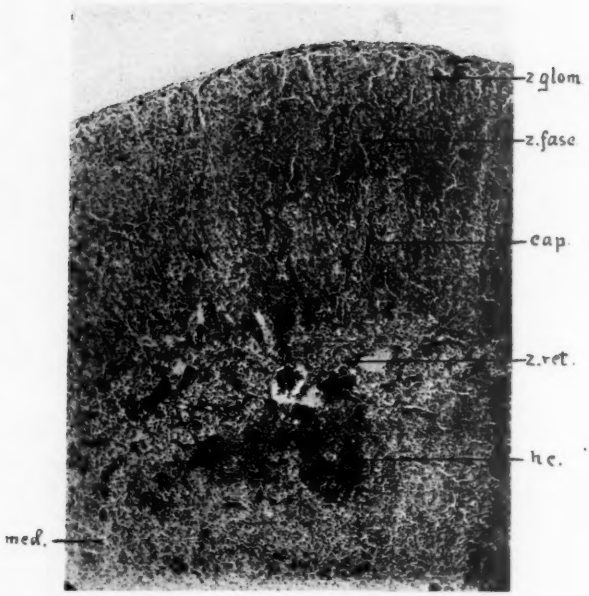


Fig. 94. No scurvy. Relative inanition. No. 186.

Adrenal. Low power. Atrophy light, hyperemia strong.

z glom zona glomerulosa, *z fasc* zona fasciculata, *z ret* zona reticularis, *med* medulla, *he* hemorrhage, *cap* dilated capillaries.

tissue, as such, having an altered proportion of calcium. Per weight unit, however, the *bone* becomes more or less calciferous according to its structure, as compact bone holds more calcium per weight unit than does spongy bone. In the dental bone TOVERUD, in the porotic rib BARDT and EDELSTEIN have proved this lessened calcium proportion. In the growth-zone of the long bones, FRAENKEL a. o. have found an increased calcium proportion by means of Roentgen examination. This is only explained satisfactorily through the author's analysis of the bone masses formed in this place by scurvy.

If the scorbutic process goes further, all bone formation ceases. The resorption, which, in the bone formed before the onset of scurvy, seems to have an ordinary extent, is seen to take place more rapidly in the bone formed in the course of scurvy, and there it gives pictures, which are similar in teeth, lower jaw and long tubular bones (Fig. 14, 34, 47 all from No. 1).

If, on the other hand, after the formation of scorbutic bone the animal receives some antiscorbutic, the osteoblasts and odontoblasts may regain their appearance and a rapid reorganization begin, which in No. 75 is evident after one day. In the tooth the reorganized dental bone gets a special character, of an irregular dentin with some few Havers' canals — osteodentin. In the connective-tissue bone hardly any difference can be seen between the reorganized bone and that formed before scurvy set in, but separating them there is a line of demarcation, staining blue with hematoxylin, in which the different bone layers often are detached when the sections are made. In the ribs, finally, parts of the pathologic bone columns are subjected to resorption, while on the base of some others new columns are formed of very nearly normal appearance.

The vascular changes observable in the bone system are described in connection with the vascular changes in other organs. Here I will only touch upon one point. HESS writes: »A marked distinction between scurvy and rickets is the paucity of blood-vessels in the cartilaginous area and in the mar-

row in scurvy, compared with the increased vascularity so generally encountered in rickets». This statement is true only with regard to the very ossification line and the adjacent portion of the marrow, and only for an advanced stage of scurvy. In the initial stage, I have found, on the other hand, and this also appears from a closer study of the records of earlier investigators, a constant hyperemia in the ossification zone, as well as in the tooth pulp. After a frame-work marrow has become formed here, the hyperemia disappears, but remains in the marrow of the diaphysis. With this statement the hypothesis must disappear, which after SCHMORL has been repeated by nearly all later investigators in this matter, that the paucity of vessels in the growth-zone should be the cause of the bone changes, more especially of the deficient melting of the preliminarily calcified cartilage.

This investigation having established the formation of a pathological bone in scurvy, the hypothesis brought out by ASCHOFF and KOCH in 1919 is no longer valid, that in scurvy the bone-forming cells would be able to form a normal bone, but that the material required, some supposed colloid cement substance, would be lacking. *Instead it is evident that the deficient bone formation is caused by a degeneration, or rather a receding of the bone-forming cells, these being changed so as to form a qualitatively more and more degenerate as well as quantitatively more and more reduced bone, till their activity eventually ceases altogether.*

My interpretation of the bone formation in scurvy, in which stress is laid upon the importance that must be attached to the gradually sinking activity of the bone cells, also makes away with several rather ill-balanced hypotheses concerning this field of investigation. So the attempts of SCHMORL a. o. to explain through entirely outward circumstances (compression) the appearance of the cartilage proliferation zone. So DELF and TOZER's supposition, accepted even by MACCALLUM, that the transversal bone column that in certain chronic mitigated cases — in fact a consequence of deficient growth and a decreasing formative power of the osteoblasts — is seen to

run along the edge of the cartilage, would itself cause the cessation of the bone formation. So the same two authors' hypothesis that this bone beam would be an attempt on the part of nature to strengthen the more and more brittle junction of cartilage and bone. Besides, it is evident that a transversally placed bone column hardly can be fit to keep together the loosening pieces of bone and cartilage, especially as the fracture is generally located a little bit closer to the diaphysis than is the beam mentioned. In order to serve this purpose a beam ought to have been placed longitudinarily over the fissure.

These hypotheses, as well as that of ASCHOFF and KOCH mentioned above, about a protecting effect of the supposed fibrin, are examples of how doubtful teleological explanations often are allowed to do service instead of an unravelling of uncertain questions through continued study.

The changes of the bone cells and the bone marrow are common to the various types of bone formed in scurvy. For the rest I wish to point out the resemblance between the structure of the new bone in the pulp, lower jaw and the periosteally formed bone of the long bones. (Fig. 10, 33, 35.)

It is noteworthy that in this receding of the higher specific functions, the result is a product that in certain respects strikingly reminds us of embryonic formations (Fig. 32 and 48). Such is the case with the frame-work marrow, with the long-remaining calcified cartilage column in the preliminary calcification zone, with the spongy character of the new jaw-bone, and with certain of the changes in the teeth, as well as with the fact that the enchondrally new-formed bone lacks collagen substance and turns a yellow colour when stained according to Hansen. This circumstance is well worth a closer study.

CHAPTER II.

The skeleton musculature. (Fig. 52—65.)

Accounts of earlier investigators are summarized, criticized or confirmed. The presence in scurvy of a myopathy is proved, which consists in an atrophy with certain characteristic features.

About the symptomatology in adult scurvy HESS writes: »The earliest sign of scurvy is usually a change in the complexion of the individual — — — he loses his accustomed vigor, seemingly becomes indolent and complains of tiring quickly, and of breathlessness». This unwillingness to move in scorbutic patients has up till now been connected with hemorrhages into the musculature or with bone changes, and this both in man and in animal. As has already been set forth, a study of my guinea-pigs fed on scorbutic diet has given me the definite impression, that we have here to deal with a purely muscular symptom, a general weakness of muscle that manifests itself in the animal's movements. Even after some joint has begun to hurt or there has been some hemorrhages, it is not these changes which alone or even chiefly give the scorbutic guinea-pig its characteristic gait, but a marked slowness and sluggishness in the muscular movements. This increases till the end. An example of this extreme weakness of muscle is the manner of death which has befallen several of the scorbutic animals, *e. g.*, No. 48 and 54. They have been overlaid by their fellows. When guinea-pigs are kept several together in one cage, they lie down by night piled on the top of each other in a small pyramid. A healthy guinea-pig seems well to endure two and even three others lying over him. But the lessened tonus in the wall of the chest of scorbutic animals does not resist the pressure. The animal is perfectly flattened down and thus suffocated. Another example of muscle weakness is the death which befell the animals No. 87 and 121, that were drowned in the milk basin. The latter only had his muzzle in the basin and seems to have lacked strength for raising its head over the edge.

The pale yellow colour, the strange lardy appearance and the weakened consistence of scorbutic muscles have been pointed out by BARLOW, and by HART and LESSING. Other investigators describe the muscular changes only in connection with hemorrhages as a lemon coloured edema (SCHOEDEL) etc. A change, not before described in detail, located in the intercostal musculature, is mentioned on p. 30.

On the other hand we find several reports of the microscopical picture of the scorbutic muscle. LEVEN found (1871) changes in the sacrolumbar and intercostal musculature in scurvy patients. In the same year other French investigators, LASÈGUE and LEGROUX, and also Hayem, observed fatty degeneration, edema and atrophy in the truncal musculature, both in connection with hemorrhages and without. In 1900, JACOBSTHAL describes the muscular atrophy as a symptom of infantile scurvy. As one cause of this he mentions hemorrhages with ensuing edema of the musculature, but does not find this explanation sufficient and therefore attributes part of the effect to the inactivity. In 1905, SATO and NAMBU found in muscles from scurvy patients interstitial hemorrhage, atrophy and degeneration of the fibres, interstitial myositis.

In 1907, HOLST and FRÖLICH published their excellent investigations on guinea-pigs. They say: »We have further, in very many cases, examined the muscles of the limbs. *The fibres of these were to a large extent more slender then usual*[1] and many of them showed some fatty degeneration. *At the same time a larger or smaller number of them were often dissolved into rows of irregular hyaline dots*[1], which did not always stain in the same way as the unaltered fibres. *Between these dots there could be seen here and there small accumulations of the multiplied sarcolemma cells*[1], but otherwise no multiplication or immigration of cells could be discovered.» In their summary and conclusions, however, Holst and Frölich say nothing about these observations, nor have I seen them reported in the literature except by Jackson and Moore.

Hart and Lessing examined in 1913 the musculature in

[1] The italics are mine.

their 5 monkeys. They found distinct degenerative changes in the skeleton muscles. »Am auffallendsten jedoch ist die Ansammlung von massenhaften, farblosen, kristallinischen Körnchen in einzelnen aufgequollenen und degenerierten Muskelfasern, die sich bei Säurezusatz lösen und bei Färbung mit Hämatoxylin eine tiefblaue Farbe annehmen. Es handelt sich um feine Kalkkörnchen.» They found no connection between fatty degeneration and calcium deposits in the muscle fibres. They say: »Um einen allgemein verbreiteten Process handelt es sich sicher nicht».

In 1919, Aschoff and Koch's large work appeared which, however, with regard to the study of the musculature in scurvy does not signify any essential advance. Concerning the framework marrow they refute successfully, as Ingier a. o. had done earlier, Looser's conception that it would presuppose hemorrhages, whereas with regard to the muscular changes they maintain this very idea of the etiological importance of the hemorrhages. As Hess seems in his monograph to accept the conclusions of Aschoff and Koch in this respect, their account must be examined in greater detail.

First of all we must note that Aschoff and Koch say about their material (p. 45): »Von der Muskulatur wurde hauptsächlich die am meisten von Blutungen betroffene Beinmuskulatur untersucht und zwar auch hier die frischen wie die älteren Muskelblutungen». It seems as if this limitation of the material deprived the authors' conclusions of all foundation with regard to the musculature where there had been *no* hemorrhage.

Further they say p. 45: »Man sieht im mikroskopischen Bild häufig von einem Blutnest zu dem anderen quer über die Muskelbündel hinüberziehende verbindende Blutstrassen, die den Eindruck machen, als wenn es sich um Blutausfüllung von in anderer Ebene liegenden Gewebsspalten handelte. Bei anderen Präparaten jedoch hat man den Eindruck, als wenn die über dem Muskelbündel verlaufenden Blutungen mit dem die Muskelfasern umspinnenden Kapillarnetz in Beziehung zu bringen sind. Auf Querschnitten sieht man, besonders in der Nähe der Faszie, öfters ausgedehnte Netzwerke von frischen

Blutungen, die jede einzelne Muskelfaser mit ihren Maschen einschneiden.» To this we may remark, that nothing is said about the hyperemia with maximally dilated vessels, frequently seen in the scorbutic muscle, and which often gives a picture like the one here described and also depicted by Aschoff and Koch (Fig. 19 in their work).

On page 46 they say: »Bei manchen Muskelfasern fällt wohl auf, dass sie sich auffallend dunkel mit Eosin färben, manche Muskelfasern sehen auch sehr viel schmäler und etwas kernreicher aus, doch hat man den Eindruck, dass es sich nur um Folgeerscheinungen infolge von Blutungen handelt». — »Schliesslich sei noch erwähnt, dass bei alten scorbutischen Muskelblutungen eine allgemeine Atrophie der Muskelfasern und eine beträchtliche Vermehrung des interstitiellen Bindegewebes beobachtet wird, Erscheinungen, die aber auf die allgemeine Kachexie und Inaktivitätsatrophie zu beziehen sind.»

The possibility that the atrophy, at least in part, might be scorbutic, is not taken into consideration. However, in the summary (p. 102) the authors do not express themselves in quite such a categorical manner. »Auch die Verfettung der Skelettmuskulatur hört nicht zum Bilde der Scorbut, sondern ist, wenn überhaupt vorhanden, durch andere Ursachen, besonders durch Zirkulationsstörungen infolge Thrombosen, zu erklären. Die Muskulatur bleibt dagegen trotz ausgedehnter Blutungen und Druck durch dieselben auffallend gut erhalten und zeigt nur stellenweise Atrophie, *wohl*[1] als Zeichen der Inaktivitätsatrophie, und *hier und da schmale junge Muskelfasern mit wuchernden Kernen.*»[1]

Herzog (1922) saw in scorbutic guinea-pigs a muscular degeneration, which in one case was very strong. She supposes, without seeming to be quite convinced, that this degeneration is caused by hemorrhages.

Already this abstract of the literature, and especially of Holst and Frölich's investigation, indicates the possibility of a primary atrophy of the musculature in scurvy. Holst and Frölich's work, however, is not unexceptionable on account of

[1] The italics are mine.

the incomplete basal diet. It has therefore seemed of importance to subject my material to a close histological examination with regard to the muscles. In most of the animals, sections have been examined from the lower end of brachium and thigh, upper and lower ends of forearm and bone, and from most costal interstices. In many cases, especially the higher numbers, only a few muscles have been examined, as shown by the records, it being considered unnecessary to extend the examination further. In general, the same sections have been used for the study of both muscular changes and bone changes.

The examined animals are divided into the following groups.

Group 1. Healthy animals without scurvy or infection. The numbers of these animals are given under the heading 6 on p. 38 The musculature shows a normal appearance, uniform colouring, fibres that are of uniform thickness.

Group 2. 23 animals with manifest scurvy without infection. 13 of these have a scorbut manifestus gravior (0 antiscorbutic), No. 1, 3, 20, 21, 23, 24, 25, 26, 28, 35, 112, 113, 115. 10 have a scorbut manifestus mitior (m. pr. d. 0,1—0.2), No. 58, 59, 65, 67, 75, 83, 86, 88, 122, 123. The former had a lifetime of 19—38 days, the latter of 32—60 days.

All these animals show distinct, most of them very pronounced changes of the musculature. These changes may be described thus.

a) Hyperemia (100 %). This is especially pronounced near the connections with tendons or periosteum, above all near the epiphyses. (Figs. 53, 54.)

b) Hemorrhages (100 %). These are always localized, of limited extent and are chiefly seen in those places where the hyperemia is strongest. Often hemorrhage has only been met with in one or two places.

c) Changes within the muscle fibre (100 %). (Fig. 55, 56, 57). The single fibrils show more clearly than in normal cases, often so distinctly that the muscle fibre as entity has disappeared. General slenderness of the muscle fibres especially near the connections with tendons or periosteum, and chiefly

near the epiphyses. Increased width of small sections of muscle fibres, which then also are homogeneous in those places, without either cross-striation or longitudinal striation, and stain dark red with eosin. These dark red, homogeneous sections are often as so-called muscle fractures seen in an otherwise tender muscle fibre. For the rest the cross-striation of these fibres is well preserved. Even in the calcified necroses of muscle fibre, described below, the cross-striation is sometimes marked through the calcium grains being layered in parallel disks.

d) Necroses of larger or smaller sections of muscle fibres or fasciculi (79 % — all except No. 65, 67, 112, 122, 123). In 9 cases (39 %) part of these necroses show depositions of grains and lumps, staining blue-grey with hematoxylin (calcium). (Fig. 58, 59, 60.)

e) Increased connective tissue (74 %). The connective tissue is often seen as strands of rounded fibroblasts, rich in endoplasm, in the place of a necrotized muscle fibre. (Fig. 56, 60.)

f) Giant-cells of a special type (96 % — all except Case 20). These cells have the appearance of big syncytial nuclei (see Fig. 55, 61, 62, 63), in connection with which there is but rarely a narrow zone of blue-coloured protoplasm. The nuclei, which always hang well together, may assume very different shapes. They stain diffusely a dark blue-black with hematoxylin. (About these, see further p. 76.)

Group 3. 5 animals without infection with scorbut latens levior, m. pr. d. 0.5—0.8, all 92 days. No. 144, 146, 151, 160, 161.

The muscle pictures are everywhere normal.

Group 4. 16 animals with infection and scorbut manifestus. 8 animals had scorbut gravior (0 antiscorbutic), 19—36 days, No. 49, 50, 54, 57, *116*, *117*, *118*, *119*, 8 animals had scorbut mitior, m. pr. d. 0.1—0.2, 17—58 days, No. 60, 66, 87, 121, *125*, *127*, 131, *132*. Of the 16 animals, 7 were infected with tuberculosis.

All these animals showed the changes described under Group 2 a and c. The other changes described there were also found in certain animals of this group, in a percentage indicated in the table below. In the first row are the 9 animals without tuberculous infection, in the second the 7 animals with such.

Table 3.

	Scorbut manifestus with acute infection	Scorbut manifestus with tubercul.
Hemorrhages . . . . . per cent.	56	43
Necroses . . . . . » »	67	86
Calcium grains . . . . . » »	33	71
Giant-nuclei cells . . . . . » »	56	86
Increased connective tissue » »	67	100

Group 5. 23 animals with infection and scorbut latens. 2 animals, No. 29 and 30, with scorbut gravior, 12 and 14 days. 14 animals with scorbut latens extensus, m. pr. d. 0.1—0.5, 15—92 days, No. *18*, 63, 120, 128, 129, 130, 135, 136, 138, *139*, *140*, *141*, *148*, *149*. 7 animals with scorbut latens levior, min. pr. d. 0.5—0.8, 18—92 days, No. 145, *147*, *150*, *155*, *156*, *164*, *165*.

One of these animals, No. 29, 12 days, showed no muscular changes whatever. Another, No. 139, m. pr. d. 0.3, 77 days, only showed some increase of connective tissue. The remaining 21 showed more or less the changes described under Group 2 a and c. If the animals in this Group 5 are divided according to the infection being acute (11 animals) or tuberculous (12 animals), we arrive at the following figures for the percentage of the gravest changes.

Table 4.

	Animals with acute infect.	tuberculous infect.
Hemorrhages . . . . . per cent.	0	33
Necroses . . . . . » »	46	67
Calcium grains . . . . . » »	27	67
Giant-nuclei cells . . . . . » »	36	67
Increased connective tissue . » »	73	92

Group 6. 3 animals with healing scurvy, No. 76, 77, 78. (Figs. 63, 64.)

These animals got a non-protective dose of orange juice, and one animal in the series, No. 75, died and showed all the grave muscular changes described above. In so far as they might have been present also in No. 76—78, these changes have nearly disappeared after a month's growing with a life-preserving dose of antiscorbutic. A certain hyperemia is left. There is an increase of connective tissue, and this tissue is rather fibrous. In Case 77, remaining necrotic muscle fragments are still to be seen. There are no giant-nuclei cells, but muscle cells lie heaped close together in a manner not seen in normal cases. Cases 76 and 77 have in some spots single giant cells of the type seen in regeneration: a large cell, rich in protoplasm, with a big syncytial light nucleus.

Group 8. 17 animals without scurvy and with an infection, which in 15 animals is tuberculous.

No. *13*, *14*, *15*, *17*, *19*, 97, *104*, *105*, *108*, *109*, *110*, *111*, 167, *174*, 176, *181*, *182*.

No. 97 and, with a certain local exception, No. 176 show no muscular changes, whereas the others show certain of the changes described under Group 2 c, *i. e.*, a swelling and homogenization of a part of the muscle fibres. There is no hyperemia, no hemorrhage, no increase of connective tissue, no pronounced necrosis, no giant-nuclei cells.

Group 8. 4 animals on relative inanition, without scurvy. No. 184, 185, 186, 187.

All the 4 animals showed certain of the changes described under Group 2 a and c, that is, a certain hyperemia, homogenization and swelling of some muscle fibres, slenderness of others and formation of giant-nuclei cells. In Case 84 (8 days) and 87 (7 days) there are only few of these, together with more numerous accumulations of muscle cells, the nuclei of which through a general diffuse dark colouring resemble those

of the giant-nuclei cells. In Case 86 (11 days) the giant-nuclei cells are more numerous, in Case 87 (14 days) still more, consequently growing in number the longer the animal has starved. No hemorrhages, no necroses, no calcium grains, no certain increase of connective tissue.

In the cases of all these 8 groups fatty degeneration of the musculature can only be stated in one case. This corroborates the conception of HART and LESSING as well as of ASCHOFF and KOCH, that fatty degeneration does not belong to the scorbutic changes in the musculature.

In 7 cases of advanced scurvy the elastin of the musculature has been stained according to Weigert without any noteworthy result.

Summary and discussion.

From this investigation it is obvious that in guinea-pig scurvy there is a real myopathy with characteristic features. Further it has become clear that the hemorrhages are of no importance to the genesis of this myopathy, even though they may secondarily and locally aggravate it. The essential change of the musculature — together with general hyperemia and local hemorrhages — is an atrophy. This atrophy appears already in the latent stage, though it can not be patho-anatomically stated as early as the changes in the teeth. It is general in the sense that it is seen in the most different muscles, though it is not uniformly extended within them, but, like the bone changes, it seems to have a predilection for certain places near the connections with tendons and periosteum (the supposed growth zone of the muscles). This scorbutic atrophy is soon combined with pronounced necroses which show a great tendency towards calcification. We also meet with a kind of giant-nuclei cells of which up till now no detailed description has been given. These giant-nuclei cells will have been observed by Hayem, by HOLST and FRÖLICH (»small accumulations of the multiplied sarcolemma

cells») and by ASCHOFF and KOCH (»wuchernde Kernen»). These investigators interpret them as being an attempt at regeneration. Large, multi-nucleated cells should, according to HERXHEIMER, be thus regarded in every case, when they appear in atrophic processes. These giant-cells are described by Herxheimer as having abundant protoplasm. Giant-cells of this type I have also observed in the healing cases 76 and 77, and I think Herxheimer's interpretation applicable to them. The giant-nuclei cells observed by me in scurvy and in inanition, call for some special remarks. These cells appear in the larger number, the longer the scurvy or inanition has lasted. They have very sparse endoplasm, in most cases there is none to be seen at all. The nucleus, which has a homogeneous colour and sometimes looks like a big irregular lump, sometimes like a syncytium of smaller, in different ways coherent nuclei. It may have the width of an ordinary muscle fibre and the length be several times the width. These giant-nuclei cells are seen in the same places, where the other muscular changes in scurvy are localized. They are often seen in the muscle fibre surrounded by a lighter zone. The descriptions above, in cases of inanition and in healing scurvy, where accumulations of muscle-cell nuclei lie close together, suggest that the giant-nuclei cells arise through the cleaving of the muscle nuclei not being completed. The rapid disappearance of these cells when the scurvy is healing is then explained through the cleaving of the cell syncytium, when the different cells at first remain lying very close together.

In these giant-nuclei cells the relation of the nucleus to the plasm, »a biologically very important expression of the vital conditions and the activity of the special cell form» (E. Holmgren), is further altered to the favour of the nucleus. This alteration is seen after insufficiency of the food in necessary nutriments (lack of antiscorbutic, general inanition), which if it goes on further, may cause necrosis. The appearance of these cells may signify, that the regeneration that is normally going on in the muscles is not altogether stopped though it does not lead to a sufficient final result.

The appearance of giant-nuclei cells in scurvy might be interpreted not as a sign characteristic of this disease, but as a sign of terminal inanition. This is gainsaid by Case 156, where during the last month there was no decrease, but on the contrary an increase in weight. About this, see further p. 131.

As to the action of an existing tuberculosis on the scorbutic muscular changes, see p. 164.

Conclusions.

1. In guinea-pig scurvy symptoms can be clinically observed, denoting that the muscles are early overtaken by the disease. This is the first clinical sign of scurvy.

2. Patho-anatomically, in guinea-pig scurvy a myopathy is demonstrable, the nature of which is an atrophy combined with necrosis.

3. The characteristics of this scorbutic atrophy is a general hyperemia, the appearance of certain giant-nuclei cells, a great tendency towards necrosis and the impregnation of the necroses with calcium, and hemorrhages in the places exposed to mechanical strain or traumata.

4. This scorbutic myopathy can patho-anatomically be demonstrated already in the latent stage, somewhat later than the changes in the teeth.

Muscles of the alimentary canal. (Tongue.)

Of these muscles I have only subjected the tongue to study. HART and LESSING have described calcium deposits in necrotic muscular fibres in the tongue of one of their scorbutic monkeys. The musculature of the tongue has been examined by me in the sections through the lower jaw, of which there is a summary p. 41. In these sections I have as a rule only found slight changes in the muscles of the tongue, and even those not very extensive. No giant-nuclei cells, no calcified necrosis. Only once a hemorrhage. It may be that a more thorough study of series of sections, in which WESTIN is now engaged, will alter this result.

Other muscles (heart). (Fig. 66—70.)

It is proved that the heart shows the same changes as the skeleton musculature.

Of other muscles I have only subjected the heart to a closer examination.

LEVEN was of opinion (1871) that in human scurvy fatty degeneration of the heart muscle is constant, and wished to explain the changes in the other organs, as also the final issue, as conditioned by this. HAYEM found (1871) astrophy, fatty degeneration and pigment, KOCH (1889) »neben hämorrhagischer Pericardit *Atrophie der Muskulatur*[1] und fettige Degeneration, sonst Blutungen unter den Pericard». In 1905 SATO and NAMBU also found *hyperemia and atrophy with increase of connective tissue*[1] between the muscle fibres. ASCHOFF and KOCH write in 1918: »Neben wohlerhaltene Muskulatur, die allenthalb stärkere Anaemie aufweist, sieht man andere Fälle, wo *eine allgemeine Atrophie der Muskelfasern, Pigmentablagerungen*[1], und wieder andere Fälle, wo eine deutliche, aber im Ganzen nur geringe Verdichtung des Bindegewebes zu konstatieren ist». They arrive, however, to the same conception as regarding the skeleton musculature, that »*das mikroskopische Bild der Herzmuskulatur abhängig zu sein scheint von dem allgemeinen körperlichen Zustande und von den begleitenden Krankheiten*».[1] As to the heart muscle of scorbutic monkeys, it is to be noted that HART and LESSING (1913) found calcium deposits also here. HART has in 1909 described the conditions of the calcification of the heart muscle, and I agree with his opinion. The literature is summarized by HESS (1921) in his monography thus: »Although hypertrophy and dilatation of the heart have been noted by several observers[2] microscopic changes have rarely been recorded. Meyer, and also Leven, report fatty degeneration of the muscle fibres, which, however,

[1] The italics are mine.

[2] I have also, in manifest scurvy in guinea-pigs, seen dilatation of the heart auricles to be constant. The examination of the ventricle walls has not been carried out with sufficient regularity to allow a conclusion.

was found by Aschoff and Koch in only one case. Sato and Nambu described an increase of connective tissue, and others anemia and pigmentation. Thickening of the pericardium and subserous hemorrhages also occur.» FINDLAY (1921) found in scorbutic guinea-pigs loss of striation of the muscle fibres, capillary congestion and an edema of the interstitial connective tissue, but did not find any collections of granules such as those described by Hart and Lessing.

I have examined the heart musculature from 19 guinea-pigs, of wich 13 had scurvy in different stages. They may be grouped thus:

1 healthy animal, No. 171.

1 animal with scorbut manifestus gravior without infection, No. 113.

4 animals with scorbut mitior latens levior without infection, No. 144, 160, 161, 162, m. pr. d. 0.5—0.8, 92 days.

2 animals with scorbut manifestus mitior and an infection, No. *132*, *133*, m. pr. d. 0.2, 43—86 days; both with tuberculosis.

6 animals with scorbut latens and an infection; 4 had scorbut latens mitior extensus, m. pr. d. 0.3, 40—77 days, No. *136*, *138*, *139*, *142*; two had scorbut latens mitior levior, m. pr. d. 0.5—0.8, 18—44 days, No. 145 and *164*. All without No. 145 had tuberculosis.

1 animal without scurvy, with a tuberculous infection, No. *109*.

4 animals on relative inanition, without scurvy, No. 184—187.

The sections have been stained, some with hematoxylin-eosin, some with cresylic violet according to Weigert or Schulz.

The healthy animal and three of the four animals with scorbut levior without infection show normal pictures of heart musculature, Fig. 66. The other 10 scorbutic animals show all, whether the disease be manifest or latent, combined with infection or not, changes in the heart musculature, which on the main are congruous and accordant with those already described with

regard to the skeleton musculature. Thus, they all have a hyperemia, without hemorrhages, and a pronounced general slenderness of the muscular fibres. In some portions the fibres are instead seen to be thickened and are at the same time homogenized, staining deeper red by eosin, Fig. 67. Except in Cases 142 and 144, the separating of the fibres into fibrils is more conspicuous than under normal conditions.

Cases 132, 133, 142 and 145, all combined with infection, show necroses of muscle fibres or bundles, and in Cases 132 and 145 these necroses are to a large extent impregnated with calcium, Fig. 68. This is sometimes arranged so as to set off the cross-striation (Fig. 69, 70). The cross-striation disappears at the homogenization, but is otherwise seen to remain long, even in the slenderest rests of fibre. The muscle cells show in every case more distinctly than under normal circumstances. They are often coarser than in healthy condition and irregular in shape, so that it seems doubtful whether they are to be called slim giant-nuclei cell or bulky muscle cells. Increase of the connective tissue is only seen in Cases 136 and 145. In the seven cases where the elastic substance round the passage of the large blood vessels from the base of the heart has been examined (No. 132, 133, 136, 138, 142, 145, 164), it appears very weak, compared to the normal. In Case 164 this atrophy can not be stated.

Case 109, on complete dietary, with tuberculosis, presents a certain slenderness of the muscle fibres, but otherwise no changes.

Among the animals on inanition, Cases 184 and 187 show normal pictures, with the exception of the elastic membranes in Case 187, as in Cases 185 and 186, appearing weaker than normally. In Case 185 typical giant-nuclei cells are visible, in Case 186 hyperemia and slenderness of muscle fibres.

Conclusion.

From this examination it is evident: 1) that the heart also is affected by the myopathy before described, the nature of which is an atrophy combined with necrosis, which

necrosis has a tendency to calcification; 2) that these changes, even necrotizing and calcification of muscle fibres, can set in already in the latent stage of scurvy.

Hereby the patho-anatomical base is given for the clinical observations of heart weakness as an early symptom of scurvy.

CHAPTER III.

Liver. (Fig. 71—78.)

The varying statements of earlier investigators about the condition of the liver in scurvy are recapitulated. As result of the author's own investigations it is established that the liver in scurvy shows constant atrophic changes.

The first author whom I have found giving an opinion about the condition of the liver in scurvy is Carl von Linné, in 1742. His utterance, though not quite clear, is yet of great interest. It is cited on page 138. In human scurvy the pathologists in the latter half of the 19th century have found very different pictures in the liver. There has been hyperemia (Lukin, Koch), anemia (Hayem), hemorrhages (Variot, Koch), clear atrophy in isolated cases (Lukin), profusion of fat (Leven, Wagner, Hayem, Koch), and so on. Sato and Nambu in 1905 report fatty infiltration and hemorrhages as well as pigment deposits along the stroma, and Urizio (1917) a slight interacinous increase of nuclei along the bile-ducts. Aschoff and Koch publish in 1919 a particularly careful study of livers from 23 soldiers who had died with scurvy. They sum up their findings thus: »Die *Leberveränderungen* in Gestalt von Atrophie, fettige Degeneration und von zelliger Wucherung im Bereiche atrophischer, fast an acute Atrophie erinnernder Läppchenveränderungen, ferner der gleichzeitige Befund von frischer Cirrhose der Leber bei Scorbut *sind zu verschiedenartig und andererseits zum Theil ein zu häufiger Befund bei anderen Krankheiten, als dass sie mit dem Scorbut in direkten Zusam-*

menhang zu bringen wären[1]*;* doch empfiehlt sich eine weitere Beobachtung des Verhaltens der Leber auf alle Fälle». Hess summarizes in 1920 the results of previous investigators. After having mentioned, how in different cases there are records of congestion, atrophy, hemorrhages, cloudy and fatty degeneration, early cirrhosis, depositions of blood pigment, he also words the conclusion thus: »In the liver no change is found with sufficient regularity to warrant its acceptance as a distinct lesion of scurvy».

Hart and Lessing found in one of their monkeys »im periportalem Bindegewebe und zwar im Lumen kleiner Gefässe zu grösseren Gebilden zusammengeflossene Kalkschollen. Die Kalkablagerungen schienen in thrombotisches Material erfolgt zu sein.»

In scorbutic guinea-pigs the liver is unanimously stated to be macroscopically normal. Several authors have missed changes even in the microscopic examination (Baumann and Howard). Abderhalden and Wertheimer declare in 1921 that they have several times observed necroses in the liver of scorbutic guinea-pigs. Their animals, however, lacked beside antiscorbutic also various other substances in their dietary. Iwabuchi (1922) found the liver columns more slender than normally.

Finally a very interesting work by Hausmann 1922 is to be mentioned. He studied the presence of urobilin in the urine of man in different stages of scurvy. He arrives at the conclusion that the urobilinuria does not seem to be directly connected with the hemorrhages but ought to be explained by the supposition of parenchymatous changes of the liver or spleen. Coincident with the urobilin there is an appearance and — in recovery — disappearance of achlorhydria in the gastric secretion, for which reason Hausmann presumes coincident parenchymatous changes in ventricle and liver.

The cautious manner, in which for instance Aschoff and Koch express themselves when judging about the scorbutic

[1] The italics are mine.

changes in the liver, is explained chiefly by the fact that very nearly all their cases have suffered from other diseases, generally tuberculosis, which as a rule cause changes to occur in the liver. This is yet another reason for trying to solve the question experimentally.

The liver in most of my animals has been carefully examined microscopically. The results have been brought together in groups.

As controls I have used the healthy animals enumerated under Group 6 p. 38. The study of the liver pictures of these animals once more proves the well-known facts that the liver cells in normal cases stain rather whimsically; that fat is found normally, as a rule sparse but sometimes (Case 10, after gestation!) abundant, and also pigment; that in the middle of an otherwise normal tissue and in an otherwise seemingly quite normal, healthy animal a small necrosis may incidentally be found in the liver, with (Case 11) or without (Case 95) connective-tissue reaction.

Then I collocated the changes found in 47 animals with manifest scurvy, in which there was no reason for supposing a complicating infection. No culture of bacteria has been made in these cases. In 12 cases, those first autopsied, the spleen has not been microscopically examined (No. 1, 3, 20, 26, 28, 43, 56, 67, 71, 83, 85, 86). The numbers of the remaining 35 are found in Group 3, p. 92. Of these 47 animals, 36 had had no antiscorbutic, whereas 11 had received a small dosage (0.1—0.2 m. pr. d.).

I began my investigations by examining the right lobe, the middle regions, and the left lobe of the liver separately, in sections stained by hematoxylin-eosin and frozen sections, stained by sudan. Of 8 cases thus examined, 5 showed identical changes in the different lobes, quantitatively as well as qualitatively. In the others the differences were inconsiderable; now the right, now the left lobe showing a somewhat greater change. In the continued investigation, therefore, sections from different parts of the liver were examined without it being established from which part they originated.

The microscopic pictures show in every case changes, that more or less markedly diverge from those of the controls. Parts of these changes are seen from the figures 72—78. As an example of the parenchymatous changes I quote the description of Case 1 (scorbut manifestus gravior, 24 days). »The acini appear atrophic. Venae central. lie much closer to each other than normally. Liver columns slender. Cells reduced in volume. Protoplasm generally faintly coloured; seems to be homogenized, with indistinct cell boundaries. In places where the staining of the protoplasm is specially defective, it shows a bright structure. The nucleus smaller than normally, appears atrophic; the chromatin, massed together in lumps, often gives a diffuse blue colouring to the whole nucleus. A number of parenchymatous cells have a more normal appearance. Pigment, resembling bilious pigment, sparse in the parenchymatous cells. Fat sparse, diffuse. The cells of the stroma are more than normally prominent. This seems due partly to the diminishing of the parenchymatous cells, partly to the increase of the stroma cells.»

The change found in all of 47 scorbutic livers is an atrophy, which is most evident in the study of the nuclei. These show in all cases an extensive karyorhexis and pyknosis. The protoplasm also is changed in the manner described for Case 1, the cells are small, the columns slender.

Fat is seen in most cases. Only in 6 cases it is absent. In 3 cases the fat is concentrated centrally in the acini, in 3 cases peripherally, but in most cases distributed diffusely. In many cases there are only isolated fat drops. In 20 cases the adiposis is more considerable.

The *connective tissue* of the stroma seems slightly increased in 17 cases. In 16 other cases the cells of the connective tissue are also prominent compared to the parenchymatous cells, but one has the impression that this is caused by the atrophy of the latter. Finally, an increase of the interlobular connective tissue can in 12 cases with certainty be excluded.

A brownish yellow (bilious) *pigment* is seen in most cases (38). Only in 7 it is abundant.

Necroses are found in half the numbnr of cases (22). They are sometimes small but often much extended and may even spread through large portions of the liver. Only in 3 cases (No. 85—87, 39—43 days, 0.1 m. pr. d.) the necroses are surrounded by connective-tissue cells. In 12 cases (26 %), the strata, depicted in Fig. 76, 77, 78 of blue-grey to blue-black grains or lumps are seen, which by treatment with sulphuric acid are proved to contain calcium. These cases are No. 7, 24, 71, 72, 73, 74, without antiscorbutic, 25—29 days, and No. 67, 70, 84, 85, 86, 122, with a m. pr. d. of 0.1—0.2, 39—55 days. Thus in cases of scorbut manifestus gravior (0 antiscorbutic), calcium has been found in the liver necroses in 6 of 36 cases, that is, 16 %, whereas among 11 cases of scorbut manifestus mitior (0.1—0.2 m. pr. d.) it was found in 5 cases (46 %). In explaining this difference we have first of all to observe the longer lifetime of the latter animals. The calcium is in the smaller necroses often distributed diffusely throughout the necrosis, in the larger ones stratified in a border zone. Fat is often seen all over the necrosis like hardly visible drops. Besides it appears in many cases as a zone of large fat drops outside, inside or together with the calcium zone, or as a solitary border zone, Fig. 75. In some cases there is also a border zone of brown pigment (not iron) round the necrosis. Thus we see necroses of different appearance, from small ones without reaction up to the very large, while in or around them brown pigment, calcium, fat and connective tissue appear in different combinations. These large necroses have an irregular form and have no regard to the acinus-delineation. A connection between their boundary-lines and any definite liver stucture is not demonstrable.

To summarize, we have thus found in these 47 scorbutic livers the picture of a simple atrophy. In some cases (No. 3, 6, 7, 58, 59) *this atrophy has been so slight and uncomplicated that its significance may be disputed. In most cases it is more pronounced, combined with degenerative changes (fat), combined with necrosis, which may be very extensive.* Thus, there are very

considerable changes to be seen diffusely in Cases 20, 21, 23, 41, 45, 53, 73, 74, 84, 85, 86. *An outstanding feature in these necroses is that they often show calcifications.*

As a third group 15 cases of scurvy were examined, which were complicated by an infection. The animals had the numbers 5, 27, 29, 31, 46, 48, 49, 50, 55, 57, all with scorbut gravior, 12—35 days; and No. 60, 63, 64, 66 and 87, with scorbut mitior, 0.1—0.2 m. pr. d., 4—39 days. It may be said briefly that all these cases show liver changes like those just described. Necroses and considerable fat deposition are present in about the same proportion in the animals with an infection, as in those without one (respectively, ca. 50 per cent. for necroses, ca. 40 per cent. for stronger fatty degeneration). This conformity must, however, be looked upon as an accidental result, as in the infected animals different factors act in opposite direction, namely the shortened lifetime and the complicating infection. If we compare animals in the two groups which are comparable with regard to the nature of the scurvy and the lifetime, we find the changes of protoplasm and nuclei more pronounced in animals with a complicating infection. The increase of the connective tissue, however, is seen among these in a smaller number of cases, 20 % against 39 %, which seems plausible. The infection was in 7 cases an infection of the upper air passages, in 2 cases pneumonia, in 1 case septicemia, in 1 case enteritis, and in 4 cases of uncertain localization. The most marked changes in the liver were found in the case with enteritis (Case 31). Even if we are justified in ascribing to the infection a great importance for the liver picture, in this case as well as in those that died early, it is as a rule impossible to decide in which degree the scurvy and in which the infection may have brought about the changes in the liver.

As another group I have placed the animals which had a carefully measured antiscorbutic dosage, 0.1, 0.2, 0.3, 0.5, 0.7, 0.8 and > 1 of the minimum protective dose. Only the ani-

mals from No. 79—178, that were not infected with tuberculosis, are here dealt with. (For the liver changes in tuberculosis, see Part IV.)

0.1 m. pr. d. Animals 120—123, 15—42 days.

Considerable changes with necroses in all cases, in the first three cases calcifications in the necroses. Very strong fatty degeneration in the first, slight in the other cases. No increase of connective tissue.

0.2 m. pr. d. Animals 128—131, 15—29 days.

In all cases strong atrophy with extended necroses, more (No. 128—130) or less (131) fat, and a trace of regeneration from the bileducts. Inconsiderable connective-tissue reaction. In Case 131 calcium deposits.

0.3 m. pr. d. Animals 135—138, 37—83 days.

In all cases atrophy with fat, and a certain regeneration with a number of round cells. In Case 138 necroses.

0.5 m. pr. d. Animals 144—146.

Heterogeneous pictures. In Case 144, killed after 92 days, only fat, otherwise normal picture. Case 145 (infection, 18 days), atrophy, calcified necroses, plenty of fat. Case 146, killed after 92 days, atrophy, not much fat.

0.7 m. pr. d. Animals 151—153.

Cases 151 and 153 (92 and 90 days), a certain peripheral hyperemia in the acini, slight general atrophy, fat.

Case 152 (infection, 22 days), foci of granulation tissue, necroses with connective tissue; the rest like the preceding cases.

0.8 m. pr. d. Animals 159—162.

No marked atrophy, not much fat, a certain hyperemia. In Case 159 a large necrosis.

$>$ 1 m. p. d. Animals 167—170, 175—178.

Case 167 (appendicitis, 8 days), not much fat, a few small necroses with connective-tissue reaction.

168, 169, 170 (killed while healthy), normal picture.

175 (infection, 17 days) some fat peripherally.

176 (peritonitis, pneumonia), hyperemia, diffuse general fatty degeneration, strong protoplasm changes (pyknosis).

177 (broncho-pneumonia, 28 days) hyperemia, some fat.

Thus we find that the manifest forms of scorbut mitior (0.1—0.3 m. pr. d.) show strong liver changes like those already described above. The latent forms, on the other hand (0.5—0.8 m. pr. d.), have less prominent or even (0.8 m. pr. d.) quite slight changes, except in complicating infections, but in such cases we are met by the insurmountable difficulty of establishing the *degree* of the etiological significance of scurvy. Yet we may be justified in drawing the inference that in these latent cases with extensive changes (*e. g.*, Case 145) the infection and the scurvy have co-operated, or in other words, that *the liver of an animal that for some time back has been without a sufficient antiscorbutic dose in its dietary and therefore is suffering from a scorbut latens mitior, is more readily injured by an infection than a normal liver, so that degeneration and necrosis set in.*

In mentioning certain cases of liver atrophy in human scurvy quoted in the literature, Hess writes that these may be explained as a consequence of the cardiac changes in scurvy. For some of my cases such an explanation might not be excluded, the atrophy in 5 of the cases (No. 43, 44, 77, 78, 88) appearing specially pronounced round the venae centrales. However, the stasis can not explain the extensive changes. *The most plausible explanation is that the hepatic cells are in need of antiscorbutic for their activity and growth, and that when this substance is lacking or deficient in the food, an atrophy of the liver parenchyma takes place.*

With regard to the constant, fairly early and very extensive atrophy in scurvy, I may mention McCarrison's hypothesis, that in beriberi B-vitamin is taken from the cells of the liver to other, rapidly growing organs. The liver in rats, pigs and cattle is found to be rich in C-vitamin (Parsons).

Nothing, however, in these experiments seems directly to verify this hypothesis as applicable in scurvy.

The four animals on relative inanition (No. 184—187) show generally normal liver pictures, and this though they have decreased in weight more than the scorbutic animals, absolutely as well as relatively to the body-weight. In Case 185, however, a number of pyknotic nuclei are seen; in Case 186 there is in the edge of the liver a fairly large necrosis and close to this a couple of smaller ones, in which small blue-grey grains (calcium) are enclosed.

For some of the animals I have calculated the weight of the liver in relation to the body-weight. This seems to me to be of greater interest than the absolute figures. The result is seen from the table below, where the first figure in each row indicates the weight percentage and the second the number of animals for which the figure is calculated.

Table 5.

Liver weight per cent. of body weight		
	No tuberc. inf.	Tuberc. inf.
Complete dietary	5.8 (9)	7.4 (8)
Basal scurvy diet	4.9 (3)	6.4 (3)
Basal sc. d. + 0.1 m. pr. d.	6.0 (3)	7.0 (3)
» » » + 0.2 » » »	6.7 (3)	9.5 (2)
» » » + 0.3 » » »	9.3 (3)	8.2 (2)
» » » + 0.5 » » »	6.0 (4)	7.7 (4)
» » » + 0.7 » » »	5.8 (2)	7.6 (4)
» » » + 0.8 » » »	6.1 (4)	12.8 (2)
» » » + >1 » » »	5.8 (8)	7.0 (5)
Relative inanition	4.1 (2)	

The conclusion to be drawn from these figures, founded on a small number of cases, is that the liver in scurvy on the whole keeps the weight relation to the body which it has

in normal cases. In tuberculosis the liver weight is relatively increased, as well in animals on complete diet as in those on scurvy diet.

CHAPTER IV.

Spleen. (Fig. 79—85.)

It is shown that besides the hemosiderosis, and sometimes hemorrhage, described by previous authors, the spleen in scurvy is the site of an atrophy of the lymphoid tissue.

Of the few and varying observations of earlier authors about the condition of the spleen in human scurvy, HESS in 1920 makes the following summary: »The spleen shares the general congestion of the internal organs. Sato and Nambu invariably found large numbers of pigment granules in this organ. Hirschsprung noted many Malpighian corpuscles, Reinert describes a true hyperplasia of the splenic pulp and others mention infarcts and subcapsular hemorrhages.» To this summary may only be added, that LUKIN among his cases describes one with simple atrophy of the spleen, and also the following quotation from ASCHOFF and KOCH 1919: »Die Veränderungen, die die Milz aufweist, sind mannigfacher Natur, aber wohl in der Hauptsache durch sekundäre Erkrankungen bedingt. Die mit dem Scorbut in Zusammenhang zu bringenden Veränderungen entsprechen hauptsächlich denen, die auch an den Lymphdrüsen zu sehen sind. Vor allem findet sich Pigmentablagerung, besonders in den Retikulumzellen um die Trabekeln. Aber auch in den Pulpazellen wird Pigment gefunden. Weiter zeigt die Milz öfters die Zeichen von Stauung, auch kleine Blutungen werden beobachtet. *In anderen Fällen findet sich Vermehrung und Umwandlung der Pulpazellen in dichtgedrängte, mehr spindelige Zellform unter Zurücktreten des lymphatischen Gewebes.*»[1] About this observation, which in the light of the present experiments becomes of great interest, ASCHOFF and KOCH say nothing in their discussions of the scorbutic changes.

[1] The italics are mine.

It must be noted that CRAMER and MOTTRAM as scorbutic changes briefly mention great atrophy of the lymphoid tissue, the thymus, the spleen and the lymphatic glands.

I have found nothing in the literature about the scorbutic changes of the guinea-pig spleen. HESS says quite shortly: »The spleen is generally normal».

The complicating effect of an infection on human material, which, as ASCHOFF and KOCH point out, nearly always asserts itself, makes the advisability of solving the problem by experimental investigation quite especially obvious with regard to the spleen.

Apart from the tuberculous animals, the spleen has been examined more closely in 88 of my guinea-pigs, 62 of which with scurvy. What Hess says about the macroscopic appearance of the spleen in scurvy holds true. It is generally normal. I therefore dwell upon the microscopic picture and for that study divide my material in different groups.

Group 1: 14 healthy animals without scurvy or infection. No. 9, 11, 12, 98, 100, 101, 102, 103, 168, 169, 178, 183.

The picture of the spleen is in all these cases normal. See Fig. 79, 83.

Group 2: 5 animals without scurvy, with an infection. No. 107, 167, 175, 176, 177.

The infection was in Case 167 a colitis, in the last three a pneumonia, which in Case 176 was combined with peritonitis. All these cases, with the exception of No. 167, show the typical picture of an infected spleen with hyperemia, hyperplasia of the pulp, catarrh of the sinus. In Case 167, on the other hand, the spleen, besides sparse lymphoid elements, shows a general hyalinization of the stroma and numerous necroses, a picture indicating a very powerful toxical effect.

Group 3: 35 animals with scorbut manifestus without infection. 11 have a scorbut mitior with a minimum protective dose of 0.1—0.3 (No. 58, 59, 68, 69, 70, 75, 84, 88, 89, 122,

123), whereas 24 have a scorbut gravior (0 antiscorbutic), (No. 6, 7, 8, 21, 23, 24, 25, 35, 37, 39, 40, 41, 42, 44, 45, 51, 52, 53, 72, 73, 74, 112, 113, 115).

The spleens of all these animals show changes which are illustrated by Fig. 80, 81, 83. Under the loupe the spleen shows a less homogeneous appearance than ordinarily; the structure seems coarse-meshed. The meshes are remaining strands of lymphoid tissue, between which the other parts of the pulp, where lymphocytic elements are nearly lacking, appear light in colour. With higher magnifying power the open capillaries in the lymph follicles stand out strikingly as bright gaps. Hyperemia in the whole spleen is constant. In the follicles it is not the lymphocytes or lymphoblasts that dominate in an advanced stage, but large starshaped bright cells with a large bright nucleus, reticulum-cells. This change begins in the periphery of the »germ-centre». These large reticulum-cells are also more than normally prominent in the rest of the pulp. The pulpa cells nearly all have an abundance of ferruginous pigment. Such pigment is also often seen in the bright smaller cells which, in the absence of the lymphocytes, fill the efferent sinuses. In some cases (No. 8, 35, 37) where the lymphocytic elements are more prominent, they have more the character of lymphoblasts than of lymphocytes. Sometimes (23, 24, 25, 26) there are numerous hemorrhages in the spleen. It seems that the hemosiderin contents in the spleen ought to be connected with the hemorrhages in the body, as it is specially abundant (Case 21, 43) or more sparse (26, 42, 70, 72), according to the hemorrhages in others organs being more or less strong and numerous.

Group 4: 10 animals with manifest scurvy and an acute infection. 5 animals have a scorbut manifestus gravior (0 antiscorbutic), No. 5, 27, 49, 50, 55, while 5 have a scorbut mitior (0.1—0.2 m. pr. d.). No. 60, 66, 87, 90, 121.

In 5 cases the reaction of the spleen is distinct with hyperplasia of the pulp and increase of the lymphocytic elements. With this picture, however, features from that described

for the preceding group are mingled. In two cases (49, 87) the lymphocytic reaction is weak or uncertain, and in three other cases (50, 60, 66) it is totally absent. In some cases (49, 66) the splenic changes described above as being typical of scurvy are not apparent; in the others (50, 60, 63, 87) they are distinct.

Group 5: 6 animals with scorbut latens levior (m. pr. d. 0.5—0.8), all 92 days, No. 144, 146, 151, 160, 161, 162. No infection.

These animals all show a splenic picture which, with regard to the decrease or almost absence of the lymphocytes in the germ-centre and the appearance of large bright reticulum-cells, agrees with that of Group 3. Yet in the follicles mitoses of lymphoid cells and lymphoid elements in the efferent sinuses are seen, even if they are larger than under normal circumstances and have a brighter nucleus.

Group 6: 11 animals with latent scurvy and an infection. 2 (No. 29 and 38) have a scorbut latens gravior (0 antiscorbutic), 8—12 days. 7 (No. 63, 120, 128, 129, 130, 136, 138) have a scorbut latens extensus, m. pr. d. 0.1—0.3, 15—64 days. 2 (No. 153, 159) have a scorbut latens levior, m. pr. d. 0.7—0.8, 29—90 days.

A hyperplasia with lymphocytic reaction, even though sometimes weak, is seen in most cases. In Cases 38, 63, 128, 130, 136, 138 it is doubtful. As to the changes described as scorbutic, they are missing in Case 38, but are marked in Case 29, as in the seven cases of scorbut latens extensus. In six of these seven cases there are numerous larger or smaller necroses in the spleen (Fig. 84, 85). In cases 120 and 130 these are occupied by blue-grey plates. (Fig. 84.)

The two cases of scorbut latens levior do not show any changes of this kind. The spleen pictures here are not to be distinguished from those in Group 2.

Group 7: 3 animals with healing scurvy. No. 76, 77, 78. Under a low power the changes are seen to resemble those

in scurvy, but with a higher power a large number of small dark lymphocytes appear between the numerous large bright reticulum-cells. These quite normal-looking lymphocytes also fill the efferent sinuses in long rows. In the germ-centres there are numerous mitoses of lymphoid cells to be seen.

Group 8: 4 animals on relative inanition. No. 184—187. Among these, the spleen picture in Case 187 (lymphadenit. submax. supp., 7 days) can not be distinguished from that of a typical splenic tumour. In Case 185 (14 days) the spleen is very nearly similar to that of a healthy animal. In Cases 184 (8 days) and 186 (11 days) there is on the other hand a general paucity of lymphocytic elements, even if there are lymphocytes seen in the efferent sinuses.

Summary. According to this examination of the *spleen* from 88 guinea-pigs, of which 62 with scurvy, this organ is, in cases of scurvy, the site of changes which may be summed up as *an atrophy of the lymphoid tissue.* To this has to be added *hemosiderosis*, and sometimes *hemorrhages.* The scorbutic spleen often shows a weak or *no lymphocytic reaction to infections.* With these *necroses* easily set in.

This splenic change can be traced already at an early period in the latent forms of scurvy. In this it is analogous to the changes in the marrow of the long bones. The analogy also manifests itself in the disappearance of the specific elements being seen preferably in the region of the most intensive cellular activity (the epiphyseal ends, the Malpighian corpuscles).

The lymphoid tissue in other places.

Different lymph-glands from a number of animals have been examined, though not from so many as with regard to the spleen. Without quoting each separate case it may briefly be stated that the changes in the lymph-glands in advanced scurvy are constant and of the same nature as is described above concerning the lymphoid tissue of the spleen. The description which SCHOEDEL gives of the frame-work marrow in

the epiphyseal ends, that it seems as if the specific elements were brushed away and only the reticulum were left, can be used as an adequate description of the changes in the lymph-glands in advanced cases.

The same changes, withdrawal of the lymphoid elements and prominence of large bright reticulum-cells, are also observable already in latent cases in the lymphoid tissue, which is found in the lungs along the bronchi and is seen like nodules at their ramifications. Lymph-nodules changed in this manner in the lungs may become the site of an abscess (Case 29), as also the lymph-glands in general, according to numerous statements in the literature, easily form abscesses, »scorbutic buboes». This has also been the case with the submaxillary gland in my animals No. 5, 30, 46, 49, 60, 63, 64 and 90.

CHAPTER V.

Kidney. (Fig. 86—90.)

It is shown how in scurvy the kidney presents two different kinds of changes, a certain atrophy, as in other organs, and besides calcium deposits that may be explained in connection with a rapid calcium excretion.

About the state of the kidneys in scurvy there are but few reports in the literature. Lust and Klochmann suppose that scurvy is due to a disturbance of the calcium excretion, without defining this disturbance more closely. The pathoanatomical findings are summarized by Hess (*l. c.* p. 102) thus: »The kidneys are often normal. On the other hand, various forms of nephritis are found, with cloudy swelling or interstitial change — a not infrequent complication of scurvy. More typical of the primary disease are congestion and hemorrhages». Hayem found fatty degeneration in this organ, and Aschoff and Koch a slight change of this kind in one case.

I have examined the kidneys in 20 of my cases. These are grouped as follows.

3 healthy animals, No. 168, 178, 183. (Fig. 86.)

The two first show a normal picture of the kidney. No. 183, on the other hand, that for some time had suffered from beriberi-like symptoms, completely gone more than a month before it was killed, showed numerous calcium deposits in the wall and lumen of the renal tubes; of which more on p. 99. For the rest the kidney seemed normal also in this case.

13 cases of scurvy.

2 of these cases, No. 113 and *119*, were scorbut manifestus gravior (0 antiscorbutic), 19—21 days, the latter with tuberculosis, though not in the kidney, the former without infection.

3 were scorbut manifestus mitior, No. 121, 131, *133*, 4 scorbut latens extensus, No. 135, 136, *139*, *142*, m. pr. d. 0.1—0.3, 21—86 days, all with an infection which in three cases was tuberculous, yet without tuberculosis in the kidney. 4 were scorbut latens levior; 3, No. 144, 161, 162, m. pr. d. 0.5—0.8, 92 days, without infection, 1 case, No. 152, m. pr. d. 0.7, 22 days, with an infection, abscesses in various organs but not in the kidneys.

These 13 cases of scurvy all show changes which in certain cases are accordant, in others not. A general hyperemia is found in all kidneys except in Cases 135, 136, 139. All without exception show an atrophy of the epithelium which first of all manifests itself in a large number of the glomeruli looking atrophic (Fig. 87). In Case 162 this is but little pronounced. Further there is an extensive pyknosis of the nuclei of the epithelium cells and a homogenization of the protoplasm, which, in the 6 cases with manifest scurvy and an infection, stains very deficiently. In most cases the connective tissue seems to be increased in the cortex.

Pronounced necroses are not seen in any case except in connection with calcium deposits. Such were present in all cases except in those two that had a scorbut manifestus gravior, No. 113 and 119. The pictures (Fig. 88, 89, 90) give an impression that here we have to deal with a different process from that described for the other organs where we may suppose as probable a secondary calcium deposit in a preceding atrophying or necrotic tissue. In the kidney the pictures are more

varying. The glomeruli, the epithelium of which seems to be most changed, are free from calcium. But it is present in the tubuli, from the tubuli contorti downwards to the collecting tubes. The calcium lumps are differently situated. Either they lie as more or less elongated formations between the capillaries and the epithelium, which they bulge out into the lumen. Or else the calcium deposits are seen in the epithelium cells themselves, sometimes in the basal part of the cell between the nucleus and the capillaries, sometimes filling the whole of a cross-section of a tubulus contortus or a looped tube of Henle. Finally the calcium concretion is seen lying wholly or partially in free lumen. In the study of the calcium masses within the lûmina one gets the impression that more or less changed epithelium cells often form part of the masses.

These pictures seem more likely to indicate a hasty calcium excretion than necroses which are secondarily calcified. Only in one case, No. 135, I have found, besides pictures like those now described, a place where a primary necrosis seems to be in course of becoming calcified. The kidneys in scurvy would then be able to exhibit calcium foci of two principally different kinds. In discussing the above-described pictures, which look like excretion pictures, it must be noted, first that the glomeruli are quite free, and then that calcium is lacking in the two cases with scorbut gravior, whereas it is present in all cases of scorbut mitior, manifestus as well as latens. See further p. 128.

It has to be investigated whether these calcium concretions in scurvy can be demonstrated through Roentgen rays. They seem to be of interest for the pathogenesis of nephrolithiasis. As a circumstance producing renal calculi excessive flesh-dietary has been stated. Might possibly the injurious circumstance be lack of fresh vegetable food?

4 animals on relative inanition, No. 184—187.

These animals show a hyperemia of the kidney. Also epithelium changes are seen in all the four cases, but they are very slight. No necroses, no calcium lumps. A light increase of connective tissue seems to take place in the cortex.

By the way may be mentioned a finding in the kidney of animal No. 183. This animal, when bought, suffered from beriberi-like symptoms (constant twisting of the neck and head to one side, difficulty in keeping balance). The animal was put on complete dietary. After a month the weight curve began to rise, after another month all clinical symptoms had disappeared. When after another six weeks the animal was killed, it seemed well, and at the histological examination no changes were found in the organs, except in the kidneys. Here there was a picture of multiple calculi, lying in the free lumen of the tubuli and under the epithelium. In fact, quite the same picture as with regard to scurvy, I had felt bound to interpret as sign of a precipitate excretion of calcium salts. The calcium metabolism in beriberi does not seem to have been especially studied. In this disease, however, a general atrophy and degeneration of different organs is recorded, which may be supposed during the active stage of the disease to retain in the body considerable amounts of calcium, excreted in recovery. It may also be mentioned that PADUA 1919 (quoted after FUNK) saw a definite relationship between beriberi and renal calculi in the Philippines. OSBORNE and MENDEL found phosphatic calculi in the bladder of a great number of rats kept on a diet, poor in vitamin A. FUNK considers (1922) all these cases to be associated with the indirect influence of the vitamins, as »it is apparent that a local infection is the real cause of this calculus formation». After my findings another interpretation will be more probable. It is possible that, as I have supposed for scurvy and beriberi, a disturbance in the state of the calcium may be the reason and that we here have to deal with a symptom of calcium excretion, which may be initial (scurvy), or setting in during the period of healing (all deficiency diseases, that have given a more considerable atrophy; see further p. 139).

Summary.

In scurvy, already in the latent stage, changes seem to occur in the kidney, which may be summed up as an atrophy

often combined with necrosis and secondary calcification, as has been described with regard to liver and spleen, though the epithelium of the kidney seems to be less sensitive than the cells of those organs. Besides there are in the kidney, in latent and somewhat mitigated cases of scurvy, calcium deposits, that seemingly ought to be interpreted as a strong calcium excretion through the kidney.

CHAPTER VI.

Adrenal.

Contrary to certain earlier won results, but in accordance with others, it is stated that in the adrenal of scorbutic guinea-pigs there is an atrophy, already seen in the latent stage, but then inconsiderable.

The adrenals have by several investigators been found without remark in scurvy in man (SCHOEDEL and NAUWERK, JACOBSTHAL, INGIER, EPSTEIN, ASCHOFF and KOCH, BIERICH). Only BIERICH found in one case the medulla increased in size. In monkeys, HART and LESSING found (1913) calcium deposits in the adrenals. In guinea-pig, several investigators have found changes in the adrenals in cases of experimentally induced scurvy. RONDONI and MONTAGNANI described in 1915 such changes in guinea-pigs, fed on cereal. They found a diminution of lipoids, atrophy and degeneration of the cortex. MCCARRISON describes how in guinea-pigs, fed on a diet of crushed oats and autoclaved milk, the adrenals increased in size and weight, whereas the adrenalin content absolutely decreased. On section he found »hemorrhagic infiltration, usually circumscribed in extent and situated around the periphery of the adrenal cortex», also »degenerative changes in the cellular elements of cortex and medulla», consisting of »vacuolation and disintegration of the cells with disappearance or loss of staining reactions of their nuclei». McCarrison's investigation seems to have been accepted unquestioningly, and it is everywhere quoted. It is, however, open to severe criticism. The investigation only comprised 5 guinea-pigs. These were fed on a dietary, where not only C-vitamin, but possibly also A-vita-

min was lacking or insufficient. The animals' lifetime is not reported, only that out of the 5 »several» died before showing clinical symptoms of scurvy. Consequently, for these animals there must have been a complication, probably an infection, and McCarrison's conclusion that the adrenal change present ought to be ascribed to latent scurvy, does not carry conviction. In another place (*l. c.* p. 347), McCarrison himself has laid stress upon the importance of excluding infection in judging the organic changes caused by vitamin deficiency. Leaving these animals out of consideration we find that 3 animals at the most with uncomplicated scurvy remain, and in these cases, as well as still more in Rondoni and Montagnani's investigations, the basal diet was not unquestionable.

FINDLAY (1921) could only in part corroborate McCarrison's findings. In scorbutic guinea-pigs he found »marked congestion both in the cortex and in the medulla. The cellular changes, noted by McCarrison 1919, were not well marked, except in those animals which had passed into a state of unconsciousness preceding death». Hemorrhage in the adrenal substance was only seen a few times, but extensive subcapsular hemorrhage was very common. — IWABUCHI reports in 1922 complementary examinations. After a diet of oats and dry milk he observes capillary hyperemia and degenerative changes in the cortex (chiefly zona fasciculata) and marrow: »Pyknos der Kerne, Aufhellen und Aufquellen der Protoplasma». He mentions that mitoses are not unfrequently seen in the zona fasciculata of scorbutic animals. Further he states a very marked disappearance of the lipoids in scurvy.

PEIPER, whose animals only got oats, also observed a diminution of lipoids in the cortex. His discovery is of a certain value because he observed a higher lipoid content when the animals had oats and orange juice; yet it may be noted that with that juice different substances, and especially different vitamins are added to the insufficient dietary. In such examinations it must be remembered how varying and labile the lipoid contents of the adrenals are even in normal cases (LANDAU).

A macroscopic change (hemorrhage) in the adrenals, I have only found once in my scorbutic guinea-pigs, above a hundred in number, though I have had an impression that the adrenals were somewhat enlarged. They have not been weighed. The adrenals of 22 animals have been microscopically examined; of these 14 had scurvy in different stages.

4 healthy animals, No. 178, 183, 188, 189, without scurvy or infection. (Fig. 92). No changes.

14 animals with scurvy.

7 of these had manifest scurvy. 4 had a scorbut manifestus gravior (0 antiscorbutic), 1 without infection (No. 113), 3 with infection (No. *116*, *117*, *118*), all tuberculous. 3 had a scorbut manifestus mitior; 1 without infection, No. 86 0.1 m. pr. d., 43 days: 2, No. 121 and *133*, 0.1—0.2 m. pr. d., 25—86 days, with an infection, in the last case tuberculous.

7 others had a latent scurvy. 3 had a scorbut latens levior m. pr. d. 0.5—0.8, 92 days, without infection. No. 144, 161, 162. 4 had a scorbut latens extensus, m. pr. d. 0.3—0.5, 59—92 days, No. 136, *139*, *148*, *149*, with an infection, which in the three last cases was of tuberculous nature.

None of the tubercular animals had any tuberculosis in the adrenals.

These 14 scorbutic animals show on the main similar changes in the adrenals, though of different degrees (Fig. 93). In no case there is any hemorrhage. A pronounced hyperemia is found in six of the seven animals with manifest scurvy (absent in No. 113) and in three of the four animals with a latent scurvy and infection. Cellular changes, consisting in pyknosis and a defective staining of the protoplasm, are found in all the 14 cases, chiefly in the different layers of the cortex. In none of the cases with manifest scurvy it has been possible to discover a mitosis, and in the animals with latent scurvy only in Cases 161 and 162. In certain cases there is a necrosis, though only of a few cells (No. 117, 136, 149). Only in Case 133 there is a necrosis of a larger group of cells. Thus, necrosis is only found in cases where the scurvy is combined with an infection. A trace of increasing inter-

stitial connective tissue is perceived in Cases 86, 144 and 161. In Case 133 it is more distinct, and besides numerous migratory cells of different types are seen round the necroses in this case.

In some cases a yellowish brown pigment is seen in the zona reticularis. In case 86 it fills the whole of the gland. For the rest there is no pigment, except in Case 113 a focus of blue-grey lumps, which might be interpreted as calciferous. I have not found any sure calcium deposit in the adrenals.

4 animals on relative inanition, No. 184—187 (Fig. 94).

These animals show reciprocally corresponding changes. First of all there is a hyperemia. The two cases that had lived longest, No. 185 and 186, also show hemorrhages in the parenchyma, localized to the zona reticularis. Cellular changes, such as are described in the scorbutic animals, are also met with in the inanition animals, but in a much lesser degree. No necroses, no connective tissue. On the other hand the inanition animals show a lively cell division. Whereas in healthy animals this must be searched for and is totally absent in animals with pronounced scurvy (Iwabuch made an observation to the contrary), we find here, specially in the outer cortex layers, numerous pronounced mitoses (this observation was made already in 1892 by MARTINOTTI, as mentioned by IWABUCHI).

Summary and conclusions.

In scorbutic guinea-pigs changes appear in the adrenals which may be summed up as a simple atrophy, at first in connection with hyperemia. These changes begin already in the latent stage, but are then faintly pronounced, as is seen by Cases 144, 161 and 162, which were killed after having received a not completely protective dose of antiscorbutic (0.5—0.8 m. pr. d.) for three months. A tuberculous infection may in Cases 148 and 149 be supposed to have aggravated the symptoms of latent scurvy.

Thus, scorbutic animals show early changes in the adrenal, but not earlier than in other parenchymatous organs. These

changes must therefore by no means be taken as a reason for placing the adrenals in the centre of the pathogenesis of scurvy. The investigation reported in these pages, on the contrary, argues against such a conception.

CHAPTER VII.

Salivary glands.

It is confirmed, as an earlier investigator has already shown, that in scurvy there is an atrophy of the salivary glands.

The only statements about the condition of these glands in scurvy that I have found in the literature are by McCarrison and Toverud. McCarrison reports that he has found the weight reduced in scurvy, compared to the normal. Toverud has in 1922 examined microscopically some of the different groups of salivary glands, though the insufficiency of the material (he does not mention the number of animals examined) deters him from pronouncing any definite statement, and he gives no details.

I have examined the sublingual gland in 39 of my cases, of which 24 had scurvy in different stages, and the submaxillary gland in 31 animals, of which 18 had scurvy. Both these glands are mixed, though the sublingual gland chiefly contains mucus-secreting cells, and the submaxillary gland chiefly serous alveoli. The examined animals are grouped thus.

No scurvy, no infection:
Sublingual gland, No. 9, 10, 11, 12.
submax. » » 168, 169, 170, 171, 188, 189.

No scurvy, with infection:
Sublingual gland, No. *15, 17, 19.*
submax. » » 167, *172, 173,* 175, 176, 177, *180.*

Scorbut manifestus gravior, without infection:
Sublingual gland, No. 1, 4, 20, 21, 23, 25, 28.

Scorbut manifestus gravior, with infection:
Sublingual gland, No. 46, 49.
submax. » » *116.*

Scorbut manifestus mitior, without infection:

Sublingual gland, No. 58, 59, 67, 75, 83, 86, 88.
submax. » » 122, 123.

Scorbut manifestus mitior, with infection:

Sublingual gland, No. 87.
submax. » » 125.

Scorbut latens gravior with infection:

Sublingual gland No. 29, 30.

Scorbut latens mitior extensus, with infection:

Sublingual gland, No. *18*, 135, 136.
submax. » » 129, 140, 141, *148*, *149*.

Scorbut latens levior, without infection:

Sublingual gland, No. 146.
submax. » » 151, 160, 161.

Scorbut latens levior, with infection:

Sublingual gland, No. *150*.
submax. » » *147*, *155*, *156*, *163*, *164*, *165*.

Relative inanition:

Sublingual gland, No. 184, 185, 186, 187.

Deficiency of A-vitamin:

Sublingual gland, No. 79, 80, 81, 82.

The mucous alveoli show an essentially different picture in rest and in activity. The animals enumerated as healthy show examples of both; so do the scorbutic animals. In both stages the former differ essentially from the latter. Healthy animals show during rest wide, extended cells, the thin walls of which often bulge sideways and also penetrate unequally far towards the lumen. The nuclei lie basally and often so far from each other that they look like separate swellings of the basement-membrane. Also in rest the cells are filled with secretion, ready for discharging it outwards when needed. In scurvy another picture appears. The cells lie in the alveoli in a circle, equally narrow, equally low, with parallel, thicker walls. The nuclei, often pyknotic, lie so closely together that

a layer of cells seems to be formed inside the basement-membrane. All activity seems to be arrested. The picture of an atrophy is present. Even when the gland is seen working and the picture in consequence is changed, the difference between the scorbutic and the normal animal is evident. The change in the scorbutic gland is not nearly so great as in the healthy. Also the serous alveoli show changes in the scurvy cases, consisting in pyknosis of the nuclei and an homogenization of the cell structure. In 4 cases of scorbut latens levior, m. pr. d. 0.8, 111—92 days, No. 160, 161, 163, 164, and in Case 18, marked changes of this nature are absent. They are seen in all the other scurvy cases. In Cases 147, 148, 149, 165, rather extensive necroses are seen in the submaxillary gland, but in all these cases there is quite close to it a caseous tuberculous lymph-gland; and as there are no necroses in the salivary glands of the other cases, it is an obvious conclusion that a local influence from the tuberculosis in the lymph-gland has caused the necroses in question. No tubercle bacilli have been demonstrable in the salivary gland, nor do the histological changes in any of these cases indicate a tuberculosis in the salivary gland.

None of the 20 animals fed on complete dietary showed analogous changes, whether they were without infection or had one, acute or tuberculous. On the other hand, some slight changes of this kind were seen in two of the four cases, the dietary of which did not include cod-liver oil, No. 79 and 80, but these two had also a scorbut levior. Such slight changes were also found in one of the four animals on relative inanition, No. 184, 8 days.

Conclusions.

1. Through this investigation Toverud's supposition is corroborated, that the salivary glands in scurvy suffer an atrophy.

2. This atrophy can be demonstrated in an early stage, somewhat later than the first changes in the teeth, but earlier than the costal changes.

CHAPTER VIII.

Lung.

Previous investigators have not pointed out any constant changes in the lung caused by scurvy, nor has the present author been able to find any.

Earlier investigators have described a variety of symptoms in the lung in cases of scurvy, without any of them being stated as constant: hyperemia, hemorrhages, hyaline degeneration of the walls of the blood vessels, edema, pneumonia. No systematic examination of the lung of scorbutic guinea-pigs seems to have been undertaken. As I had not planned any such examination at the outset, no case of scorbut manifestus gravior has been examined. The 19 animals, the lungs of which have been examined, are grouped thus.

2 healthy animals, without scurvy, No. 168, 171.

4 » » » » , with infection, No. *109, 173*, 177, 179.

The animals show a normal lung picture.

2 animals with scorbut manifestus mitior, 0.2 m. pr. d., 43—86 days, No. *132, 133*, both with tuberculosis.

4 animals with scorbut mitior latens extensus, 0.3 m. pr. d., 40—83 days. Two with tuberculous infection. No. *139, 142;* two with acute infection, No. 136 and 138.

3 animals with scorbut mitior latens levior, 0.8 m. pr. d., 92 days, No. 160, 161, 162.

Already under a low magnifying lens some of the scorbutic cases show a widening of the respiratory bronchioles and their ramifications, with thin interalveolar septa (Case 133, 139). In other cases this picture which looks rather like emphysema, is not distinctly apparent or is altogether lacking. A close study of the elastic tissue stained with cresyl-violet according to Weigert or to Schulz has not shown a congruent result. In certain cases it seems somewhat weaker than that of the normal cases, in other cases not. A study of the lymphoid tissue, which follows the ramifications of the bronchial tree, showed the atrophy described above. When a local

infection supervenes (*e. g.*, Case 139, bronchitis), the number of the lymphocytes may again increase.

However, all these changes taken together have not been sufficient for gathering a picture of the scorbutic lung, which would allow us to single out these preparations from the lung pictures of normal cases. Thus I have not found any change in the lung tissue that I can call pathognomonic. As the research has not been sufficiently comprehensive, it will be continued.

In *4 animals on relative inanition*, No. 184—187, there was an atrophy of the elastic fibres of the lungs, most pronounced in the two animals that had lived longest (No. 185 and 186).

Summary:

Considering the statement of RHEINDORF in 1918, that the elastic fibres in the skin perish early in scurvy, and the observation of atrophy in the elastic membranes around the large vessels of the heart, which I have described, a similar change in the lungs might have been expected. However, it could not be stated in the animals examined.

CHAPTER IX.

Blood and blood-vessels. Hemorrhages in scurvy.

In scurvy there is, according to the results of previous investigators, a deficient regeneration of erythrocytes and polymorphous leukocytes, an initial hyperemia and a weakness of the vascular wall. This weakness is explained by the present author as a defective formation of the collagen connective tissue of the vessel and the lack of sufficient support from the atrophic tissue outside the vessel.

As a result of the investigations of later years we may set down that the cause of the hemorrhages in scurvy is a weakness in the vascular wall and not changes in the blood (HESS, BEDSON, TOBLER, UMBER a. o.). Yet it may be mentioned that some few authors think they have been able to state a decreased number of platelets (WASSERMANN and KIRCH) or an prolonged coagulation-time (BRANDT).

The cells of the blood, however, offer certain interesting features. The red blood-corpuscles, it is true, are sometimes in manifest scurvy normal in number (Brandt's observation of a polycythemia is isolated), the hemoglobin 100 per cent. (Tobler), but when complications set in (hemorrhages, infections), the number of blood-corpuscles and the hemoglobin are apt to sink (many investigators, most recently Salle and Rosenberg) and can afterwards only with difficulty be brought to rise, till antiscorbutic is administered. But then the effect of the antiscorbutic is amazingly rapid, a matter of a few days. *The regeneration of red blood-corpuscles* thus seems to be *insufficient in scurvy*, which becomes manifest only when the demand is raised.

It is the same in the case of the white blood-corpuscles. They have often been found normal in scurvy (Herzog, Koch, Umber, Bedson a. o.). Numerous investigators (Naegeli, Leitner, Bierich, Salle and Rosenberg, Haussmann) have stated a leucopenia or in any case a failing leukocytosis in scurvy patients with infections, when a strong leukocytic reaction might have been expected. In film preparations of bone marrow, neither Hart and Lessing nor Fraenkel have been able to find abnormal cell forms. In Giemsa-stained preparations of marrow from the long bones of guinea-pigs in different stages of scurvy I have also stated that fact. Thus *in scurvy the regeneration organ of the polymorphonuclear leukocytes seems also to suffer from a weakness*, which becomes manifest when the demand is raised.

As to the conditions of the vessels, I have already remarked that when Hess establishes the failing vascularization of the frame-work marrow as the distinguishing mark between scurvy and rickets, this is true only of far advanced cases of scurvy. In initial cases there is everywhere a *hyperemia* in the growth zone of the bones as well as otherwise in the marrow and in other organs (Herzog, Findlay, Iwabuchi, Toverud). I have met with this hyperemia in all examined organs, and I have also found it to be an early symptom. The authors just mentioned unanimously state it to be a dilatation

of capillaries and veins, and this observation I have also found to agree with the conditions of my scorbutic guinea-pigs.

Iwabuchi sets forth that this dilatation of the veins can become so strong that at first sight it gives the impression of being a hemorrhage. This I have been able to verify, especially in the adrenal and the bone-marrow. When furthermore the general fragility of the organs in scurvy is considered, which easily causes artificial changes in the continuity of the vascular walls, special attention must be paid to the differential diagnosis between hyperemia and hemorrhage. The description of some earlier investigators suggest that they have not sufficiently taken this into consideration (McCarrison, Aschoff and Koch). Whether the hyperemia in scurvy is due only to the weakness of the vascular walls or of the heart, or whether an irritation from products of atrophic cells is of any account, I leave unsaid.

Hart and Lessing, and Ingier describe the presence in scorbutic vessels of »hyaline thromboses», to which v. Recklinghausen attaches great importance. In my scorbutic guinea-pigs, these »hyaline thromboses» are seen in every case. They are, however, also found in healthy animals, though to a smaller extent. Like Ingier I feel inclined to look upon them as post-mortal formations. Differences in the sinking velocity or in the sinking time of the red blood-corpuscles in scorbutic and healthy guinea-pigs may be the reason of their more frequent presence in the scurvy cases.

Hemosiderin has been found in different organs by a large number of previous investigators. The results of my investigations in this respect agree with those of Iwabuchi, that sparse hemosiderin is found locally, where there has been a hemorrhage, but for the rest in a larger quantity only in spleen and bone-marrow.

With regard to the localization of the hemorrhages, my observations completely agree with those of earlier investigators in that they are chiefly seen where an intense proliferation with congestive hyperemia takes place, as in the neigh-

bourhood of the epiphyseal lines in the long bones (JACOBSTHAL, SCHMORL, FRAENKEL, LOOSER).

Yet I am not disposed to ascribe this circumstance exclusively to the congestive hyperemia. In these growth zones a lively rebuilding takes place, also of the vessels, with strong resorption of old tissue and a vigorous new growth. When now, as in scurvy, the apposition declines until failing (see »Pathogenesis», p. 133), the effects of this ought to become manifest first of all in places where the resorption is the strongest, which is exactly in the growth zones. This explanation, which supposes the latent period of scurvy in a tissue to be the shorter, the livelier the growth is of this tissue, may also be applied to the circumstance that the latent period of absolute scurvy is the shorter, the more rapidly an individual grows; for young guinea-pigs 2 weeks, for young monkeys 2 months, for infants longer and for adults of different species a longer time than for growing individuals.

The hemorrhages, a consequence chiefly of the weakness of the vascular wall on account of deficient new growth, are thus coordinate with other symptoms in scurvy. BARLOW, KOCH and LOOSER, would assign to them a more central position as directly causing all other scorbutic changes, specially those in the bones. With regard to these the opinion of the authors in question has been proved to be erroneous by Schoedel, Schmorl, Fraenkel, Ingier, Aschoff and Koch. Concerning the musculature and the parenchymatous organs I have been able to state the same. The hemorrhages may aggravate the scorbutic atrophy locally in these organs, but as a rule they do not give rise to it.

In tuberculosis, complicating scurvy is feared, says KOCH, on account of the frequent hemorrhages in lung and intestine which then set in. In most of my guinea-pigs infected with tuberculosis that had scorbutic diet, I have found extensive hemorrhages near the primary focus in the musculature of the thigh, around tuberculous foci in spleen a. s. o.

In 1880 SWIDERSKI (quoted after Koch) indicated as cause of the hemorrhages an obstruction of the smaller vessels through

swollen endothelial cells. Swiderski notes that in scurvy the small arteries are dilated, the veins collapsed, which may agree with his hypothesis, but not with the actual facts. Koch considers Swiderski's endothelial swelling to be a post-mortal process, »jedenfalls für ebensolche Ausnahmen, nach welchen man eifrig fahndete, weil sie die Transsudation nach dem Schema der Stauungswassersucht zu erklären gestatten würden». Lately FINDLAY, without mentioning Swiderski, after an investigation on guinea-pigs repeated his statements and conclusions: »The absence of vitamin C from the diet of the guinea-pig leads to swelling and degeneration of the capillary endothelium. As a result of this swelling of the endothelium the flow of blood through the capillaries is retarded and extreme congestion occurs». — »The tissues are insufficiently oxygenated and death occurs.» In the beginning of his paper Findlay has stated, however, that the congestion does not only befall the capillaries but also the smaller venules. According to other authors and my own research, dilatation sets in even in quite large veins. How an obstruction of the capillaries is capable of dilating the veins, Findlay has omitted to explain. I have also been able to observe changes of the endothelial cells in the vessels, namely a fatty degeneration of some cells, but this change is not constant and does not occur extensively enough to be deemed essentially important. That IDE in three out of four examined Barlow cases has found changes in the medium-sized arteries, which changes he designates as endarteritis obliterans, and has not been able to find them again in guinea-pigs, may be mentioned for the sake of completeness.

In the study of my preparations I have had my attention directed to the vessels. I have often been able to confirm JACKSON and MOORE's observation that the vascular wall has seemed to be thin, both in the arteries and veins. Even in rather large vessels the cells in the vascular wall do not lie close to each other, and between them occasionally a red blood-corpuscle may be seen. In staining with cresylic violet I have not found any atrophy of the elastic tissue, such as

RHEINDORF has presumed with regard to the skin, except in the elastic membranes around the efferent vessels of the heart. But in staining on collagen according to Hansen, on the other hand, a considerable atrophy of this tissue is observed. As collagen fibrils partly constitute the walls of even very small vessels and are likely essentially to give them their firmness, this partial disappearance of the collagen fibrils must be considered an important factor in the pathogenesis of the hemorrhages. In the next part of this work will be shown that this collagen atrophy more or less overtakes all connective tissue. Besides the direct weakening of the vascular wall in the manner indicated, a certain influence ought perhaps also to be ascribed to the general atrophy with shrinking of the organ cells under the absence of normal connective-tissue reaction. Through this organ atrophy, the vessels will lack the outer support for their atrophic wall, without which the pressure from the inside must have a still greater effect.

That local irritations (SAXL and MELKA; *cf.* above, about tuberculosis) as well as static and traumatic circumstances and a physiological hyperemia can call forth hemorrhages in a vascular wall changed in this manner, seems explicable, without these circumstances therefore being counted as anything but accidental causes. Nor are we entitled to suppose with ASCHOFF and KOCH, that because the parenchymatous organs show fewer hemorrhages than the sustentacular tissues, they would be less struck by the scorbutic changes. The lesser mechanic strain on these organs is a sufficient explanation of the hemorrhages being less prominent within them.

Summary.

Previous investigators have demonstrated the presence in scurvy of 1) a deficient regeneration of red and white blood-corpuscles, 2) an initial hyperemia, and 3) a weakness in the vascular walls leading to hemorrhages, chiefly localized in places where the growth is lively.

The last two of these observations have been corroborated by me. As an explanation of the latter serves the circum-

stance, pointed out by me, that the collagen connective tissue of the vessels gets atrophic in scurvy. As a possible contributory cause I have noted the lessened support from the atrophic tissues.

X.

Connective tissue.

A general atrophy in scurvy of the connective tissue, and especially of its collagen substance, is proved.

In the study of the histological pictures of different scorbutic organs it is easy to observe that the connective tissue seems atrophic. This is specially manifest with regard to formations, the thickness of which in sections from scorbutic and from healthy guinea-pigs can be directly compared, as ligamentum circumdentale (periodontium), adventitia of vessels, perineurium, membranæ propriæ of acinous glands, trabeculæ in the spleen and the collagen fibrils in the papillæ of the tongue. By staining according to Hansen, which shows the collagen sparklingly red in sections from healthy animals, it is found that just the *collagen* in scurvy is specially badly developed. This circumstance I have already mentioned concerning cartilage and bone, in which also the collagen is less developed or even lacking. A failing differentiation of the fibroblasts with inability of forming collagen fibrils is described p. 160 as characteristic of the reaction to tuberculosis of a scorbutic organism. A diminished development within the organs (lymphoid glands, liver and spleen have particularly been examined) of the collagen connective tissue I have been able to state already in cases of scorbut latens levior. This atrophy of the connective tissue will be a contributory cause of the loosening of the teeth and the appearance of hemorrhages.

As in the bone, I have also sometimes in the place of the collagen in sections, stained according to Hansen, from scorbutic parenchymatous organs, especially spleen, found yellow fibrils which possibly may be interpreted as pre-collagen. The collagen is often seen as a lump near the nucleus, while

the formation of elongated fibrils has failed. Before the formation of collagen is completely arrested, there is thus a stage when it is very unevenly distributed and irregularly arranged.

It is related by several early authors that old bone fractures at the onset of scurvy have become softened. The deficient callus-formation at fractures in scorbutically changed bones is also a common observation in the study of experimental scurvy. Also for the explanation of these circumstances, the pronounced atrophy of the collagen connective tissue in scurvy is of interest. Even if, as CARRELL has pointed out in experiments (1921), the cicatrization of wounds apparently is initiated not by an internal but by an external factor, the answer of the organism to the irritation is decided by internal factors. That a supply of full antiscorbutic dose is necessary to an answer of normal intensity, may be concluded from this investigation.

A general insufficiency in the collagen formation is not, as far as I know, earlier described.

PART III.

CHAPTER I.

Scurvy and infection.

I. Complicating acute infections in my animals.

Of my 189 animals about a third (60) have suffered from complicating acute infection. In the majority of cases it has been an acute infection of the upper respiratory canal. Pneumonia has been found in 13 animals, enterocolitis in 5, septicopyemia in 8, peritonitis in 1, necrosis of pancreas in 1. No wide-spread epidemic has occurred. As remarkable may be mentioned the appearance of pneumonia in 4 of the 8 animals in Series 34. In Series 29 two animals showed abscesses in the spleen.

It may be mentioned that I have not in any case found any coccidiosis. The liver was examined in nearly all cases.

II. Influence of acute infection on scurvy.

Since the hypothesis of scurvy as being an infectious disease has more and more had to yield to the vitamin hypothesis, attempts have been made to represent the infection as a necessary factor for bringing about manifest symptoms in an organism changed through lack of antiscorbutic. The reasons for these attempts are the same circumstances that caused the supposition of an altogether infectious etiology: 1) the »endemic» occurrence in certain cases, 2) the presence of acute infections in connection with the onset of the disease, and 3) the so-called scurvy fever. With regard to these circumstances the following observations may be made.

Ad 1). The endemic occurrence in persons with identical or similar dietary is more satisfactorily explained by the vitamin hypothesis.

Ad 2). That certain acute infections may have an influence on the arising and course of scurvy, is certain. ASCHOFF and KOCH state that every powerful infection in a patient with old scurvy calls forth new hemorrhages. SALLE and ROSENBERG mention that dysentery, typhoid and malaria aggravate the scurvy. Yet they have only a small number of such cases at their disposal. BIERICH saw in his large material a predisposing influence only of abdominal typhoid and dysentery, but not of tuberculosis, lues, polyarthritis acuta, or malaria. This action of diarrhea diseases has already in 1907 been observed by HOLST and FRÖLICH. »Diarrhea creates very often a predisposition to scurvy».

Several authors could verify this during the last war, and HESS dwells in 1920 specially on this fact. Concerning infants the same thing has been observed by, among others, VOGT and WALLGREN. LEICHTENTRITT and ZIELASKOWSKI write in 1922, that »chronische Darmerkrankungen — gleichgültig ob infectiöser, alimentärer, konstitutioneller Grundlage — dem Scorbut

die Wege ebnen und infolgedessen geradezu als 'Barlow-trop' aufzufassen sind». It is near at hand to connect this circumstance with an action in the intestinal canal on the antiscorbutic from abnormal products (oxidizing?).

Concerning other infections there are no certain observations in a positive direction recorded in the literature. Two of my guinea-pigs, No. 50 and 55, see charts Fig. 105 and 106, pp. 186, 188, are examples of how scurvy seems to proceed in the manner determined by the food, independently of an intercurrent acute infection. Such an infection seems in these cases to have caused a decrease in weight, which gives to the curves of these animals a course different from those of the other animals in the same series. The decrease yields place to an increase, however, and it is then found that the curves go rising towards those of the other animals, and bend downwards with these, as the animals also proceed to death at the same time as their fellows.

The influence of certain acute infections on the onset and progress of scurvy can thus be limited, partly to diseases that bring about intestinal disturbances, in which a direct action on the antiscorbutic before its resorption will easily be concluded, partly to causing hemorrhages in certain cases of already scorbutic patients. It does not seem surprising, with the already described weakness in the vascular walls, more particularly explained by me, that a hyperemia and thereby raised demands should call forth a hemorrhage. This may also be caused by other incidental circumstances, for instance trauma, or set in without any demonstrable cause.

Ad 3). The scurvy fever has always at closer analysis showed itself explainable either as a resorption fever in connection with a hemorrhage (Finkelstein), or as a consequence of a complicating infection, whereas the scurvy as such proceeds without fever, which has also been stated experimentally (Jackson and Moore).

In the case of my guinea-pigs I have not taken the temperature, and I have as a rule made no cultures of bacteria. Clinically, at the *post-mortem* and the subsequent histological

examination, an infection was stated in 22 out of 86 animals with manifest scurvy. Thus, in nearly 75 per cent. of the cases with manifest scurvy no signs of infection could be found. On the other hand, more than half the number of animals that had latent scurvy, suffered from an infection, without manifest symptoms being called forth through this circumstance.

As a result of this it may be emphasized that there are no sufficient reasons for ABELS' hypothesis, quoted above, about an infection being necessary for the scorbutic symptoms to become manifest. The circumstances which are the foundation of Abels' hypothesis might instead be expressed thus, that scurvy in man often has not had time to become manifest before an infection comes on as a consequence of the immunity being lowered by the scurvy. If, like Abels, one wishes to call the lessened resistance of the body to infections by the name of dysergy, this is quite as legitimate as many other attempts to conceal with a fine name that a thing is still incompletely investigated. To establish the dysergy as a latent stage, distinct from the manifest, is in any case unwarranted.

Thus infection in scurvy is generally to be regarded as a concomitant symptom as well as the hemorrhage. These two show besides many analogies.

1. They may both be regarded as following the scorbutic atrophy, *viz.*, the atrophy of the vessels and of the various organs that protect the body against infections.

2. Both appear in the later stages of scurvy spontaneously, the hemorrhages after physiological action, for instance contraction of the muscles, the infection without any contagion being possible to state. In an earlier stage of the disease, however, a greater injury is needed, either a violence that leads to hemorrhage, or a pathogenic bacterium that gives rise to infection.

3. Both may aggravate the scurvy symptoms, the hemorrhage by causing necroses, *e. g.*, in the musculature, the infection by acting upon the antiscorbutic in the intestine. They may also mutually educe each other, the hemorrhage becoming a *locus*

minoris resistentiæ, that becomes purulent, the hyperemia, called forth by the infection, causing hemorrhages from the weakened vessels.

4. To both, though ordinarily only concomitant symptoms of scurvy, a decisive influence on the genesis of the scurvy has been attached. The hemorrhages have been considered (Barlow, Looser a. o.) to call forth all other changes; earlier, the infection has generally been considered as representing the whole etiology, and lately (Abels) as being necessary for the passing of scurvy from a latent to a manifest stage.

III. Influence of scurvy on immunity and resistance against infection.

The numerous statements in this question are summarized in 1920 by Hess in the following way:

»The latent scurvy increases the susceptibility to infection and intensifies the severity of all medical and surgical diseases.» — »Indeed, one of the striking and important symptoms of scurvy is the marked susceptibility to infections (furunculosis, nasal diphteria, grippe, bronchitis, pneumonia). Pneumonia is one of the most frequent complications and causes of death. This susceptibility was noted by the elder authors in relation to adults. — Following the infection, the lymphnodes may become purulent, as is so frequently mentioned by the elder authors.»

»Der scorbutische Organism», write Leichtentritt and Zielaskowski in 1922, »ist nicht imstande, auf bakterielle Einwirkungen Abwehrreaktionen aufzubringen. Als Ausdruck dafür sind die kaum zur Heilung zu bringenden Furunculosen und torpiden Hautgeschwüre mit ihrer schlechten Neigung zur Granulationsbildung anzusehen.» According to Koch this is a current observation, quoted by many elder authors. Nassau and Singer emphasize how in scurvy there is seen as well a lowering of the immunity with more frequent infections, as a diminished resistance with a more malignant progress of infections. For this Abels has invented the word dysergy.

With regard to the number of the acute infections in my material, the following figures may be quoted.

Of the 62 animals, that I had put on absolute scorbutic dietary, basal diet without any antiscorbutic (scorbut gravior), 18 (29 %) showed signs of acute infection. Of the 72 animals, that had a certain, but not sufficient dose of antiscorbutic (scorbut mitior), 34 (47 %) showed such signs. The corresponding figures for the animals on complete diet are 9 out of 45 (20 %). In judging of these figures we must consider the essentially different lifetime, which for animals with scorbut mitior is twice, and for those on complete dietary three times that of the animals on absolute scorbutic dietary.

Of the groups that had 0.5—0.8 of the minimum protective dose and thus a scurvy which still at the conclusion of the experiment after 92 days was latent, in all 24 animals, only 8 were alive at the end of the experiment. Of the others, 13 (54.2 %) had died with signs of acute infections. Of 40 animals that had had complete dietary, 29 were alive and in good health after the same length of time. 8 had died of acute infection and 1 had pneumonia when killed (in all 22.5 %). The animals that had latent scurvy thus showed about twice as many infections leading to death than those on complete dietary.

With regard to all figures here quoted it may be said, that they are not founded on a uniform material, as the animals were kept in 12 different cages and thus were exposed to different infections. This remark is just and renders it impossible to divide the animals into smaller groups or to attach too much importance to the figures quoted. They might, however, authorize the conclusion, that the increased disposition for being afflicted by infectious diseases, which has earlier been noted in scorbutic patients already in the latent stage, is apparent also in my material.

The infections in Series 33 and 34, that had 1.2 and 1.6, respectively, of the calculated minimum protective dose, give occasion to a remark. Of 8 animals in each group, 2 died of acute infection in the first, 4 in the second. Here we might

advance the supposition that, though no patho-anatomical changes in these animals are found that might imply scurvy, except an uncertain hyperemia in the tooth pulp, yet the dose of antiscorbutic would not be fully protective. If so, there would exist an initial stage of scurvy, where no distinct histological atrophy, only a functional weakness in the highest developed cells would be present. The infections in question might be an expression of such a weakness. This possibility is not to be excluded. In guinea-pigs with scorbut gravior the first week probably is such a stage. With regard to the parallelism of the stages, such as they are seen in scorbut gravior from the onset till the manifest symptoms appear, with those stages that are called forth by giving different, smaller and smaller doses of antiscorbutic from the beginning, such a stage may even with probability be expected, if a dose is given which is barely sufficient to ward off the histological changes. The difference between this dose and one which assures full vigour from an antiscorbutic point of view, will be made clear by physiological investigations. Such a stage ought appropriately to be called *scorbut initialis* or *functional scurvy*.

The investigations which have aimed at finding the cause of the lessened resistance in the scorbutic organism against infections, are few. ZILVA examined in scorbutic guinea-pigs the amboceptor and agglutinin titers of the blood and the complement activity; he found these unchanged. This does not exclude, however, that, as is the case with the number of blood cells, a raised demand reveals a weakness in the regenerative power. FORTENATO found in 1921 the opsonic index lowered in scorbutic guinea-pigs. LEICHTENTRITT and ZIELASKOWSKI examined the trypanocid substance of the blood in scurvy and found it lessened. Their experiments are too few in number to allow any sure conclusions to be drawn. I have not undertaken any corresponding investigations. In this connection, however, I may recall the result of the histological examination of the lymphoid tissue in my cases of scurvy, complicated by acute infection, as far as it has been examined. (See page 93, 94).

It seems we may conclude from this that the lymphoid tissue in scurvy reacts tardily to infections. In this atrophical state of the lymphoid tissue as well as in the changes of the bone-marrow we may have to seek one foundation for the inferiority of the scorbut organism in the struggle against infections.

CHAPTER II.

Disposition and scurvy.

That different rapidity of growth, thus also different ages, dispose differently to scurvy is established and founded on the very nature of the disease. The »disposition» to scurvy which is found in individuals with intestinal disturbances, may be explained as due to an external factor — probably destroying of antiscorbutic in the intestine.

Apart from these two circumstances we know nothing with certainty about the disposition to scurvy in different persons. Many authors have presumed such a disposition, it is true, but they seem to forget that the diagnosis in this case is a diagnosis of elimination, and that among the external factors that are to be excluded, are the following: the age of the food (milk) before it is consumed, the preparation of food in the kitchen, a careful determination of the quantities consumed of the substances that may contain antiscorbutic, control of the nurse.

FINKELSTEIN'S oft-quoted case (a pair of twins) does not fulfil these claims. Another account of the same author of how 3 children with the same nurse had scurvy one after the other, whereas no other children in the department had the disease, without the external factor, which nevertheless must be supposed to have existed, being discovered, invites to caution. Nor do we learn with regard to WIELAND'S twins, of which one had scurvy and the other not, which quantities they each of them consumed. But in the absence of an exact statement about this the explanation may be thought to be the same as has been given by CHICK and HUME of the state-

ment of McCollum, Pitz etc. which were at variance with the results of other authors. The American investigators had not observed that the guinea-pigs took unequal quantities of raw milk, which contained a certain amount of antiscorbutic. Some of them had scurvy, while those who took sufficiently were protected.

Another example of a precipitate conclusion with regard to a disposition (psychical) is given in Bierich's description of a number of scurvy patients who appeared greatly depressed in the hospital. When they had been removed to a forest sanatorium, where they were allowed to cultivate and harvest their own vegetables, both their spirits and the scurvy improved. Bierich thinks, as so many older authors have thought, the better spirits to be the probable cause of the recovery. It is likely, however, that also the vegetables in the forest sanatorium were better from the antiscorbutic point of view. Bierich has made an excellent exposition of his large material, but it gives him no right to the conclusion he draws from it, whether his supposition of the psychical influence may be or may not be found correct.

Conclusion.

Irrespective of the cases which are connected with an unequal rapidity of growth, and those connected with intestinal disturbances, no endogenous factors predisposing to scurvy have been established. The existence of such factors, except those mentioned, must be looked upon as altogether hypothetical.

CHAPTER III.

The latent period of scurvy.

Scorbut gravior has a progressive course from beginning to end. Also scorbut mitior, where the organism receives a certain degree of protective dose, has a progressive course, old tissue being constantly resorbed without being replaced by new of full quality. Even in the latent cases, therefore, the

long bones for instance become more and more brittle. The moment when a latent stage passes into a manifest is for each case determined by the relation between the atrophy of the tissue and the demands made on it. A violent blow may, for instance, by causing a fracture reveal a scurvy which without this accident might still have been latent for a long time. It is the same with a hemorrhage caused by an infectious hyperemia. From this it is obvious that the line of demarcation between latent and manifest scurvy is movable. Most authors also suppose the presence of an intermediary stage between the latent and the distinctly manifest stage. FRAENKEL states that »bei einem nicht geringen Prozentsatz der Fälle welche unter dem Diagnose Darmkatarrh mit Anaemie, Pädatrophie u. dgl. mehr segeln, sich mancher Fall von Barlowscher Krankheit verbirgt». HEUBNER expresses himself to the same purport. EPSTEIN, HESS and also FRANK state that the growing in height is already during this period arrested in children. ARON denies the presence of such an initial stage, but in this he stands alone against KOCH, SCHOEDEL, HART and LESSING, FINKELSTEIN, L. F. MEYER, CHICK and DALYELL, the above-mentioned authors and all other investigators of mark who have written on the subject.

If thus the supposition of a clinical stage, during which the diagnosis of scurvy often can be made only for the therapeutic effect of antiscorbutics, seems to be well founded, my research has afforded the possibility of understanding this better. Not only in the teeth and the bone-system, but also in muscles, liver, spleen, kidney, salivary gland, adrenal, and probably in other organs, already in the latent stage more or less severe changes appear, which together constitute the scorbutic atrophy of the organism. This atrophy is progressive and gives manifest symptoms after a length of time that varies for the different cases.

The duration of the latent period thus bears a relation first to the antiscorbutic dose given and then also to outward circumstances. In guinea-pigs the latent period is, approximately, with no antiscorbutic 1 week, with 0.1 of the minimum

protective dose more than 2 weeks, with 0.2 m. pr. d. more than 3 weeks, with 0.3 m. pr. d. about 10 weeks, a. s. o. When the dosage of antiscorbutic approaches the completely protective dose, marked clinical symptoms never appear, only indistinct signs of general ill-health. Indeed, I think it very probable that there is a stage of scurvy, when not even patho-anatomically any pathognomonic changes are demonstrable in the teeth, but when nevertheless the promptness with which the vital functions of the body take place is lowered, a scorbut initialis or functional scurvy. ZILVA argues in the same direction.

HESS writes: »There is no doubt a considerable number of infants, who quite unknown to any one pass through the state of latent scurvy. If this large group of cases were included in the incidence of infantile scurvy, we should not look upon it as a disorder, which occurs rarely during the first six months of life.» However, it is probably the same also with other ages in districts, where during certain periods there is only a limited supply of foodstuffs, valuable from the antiscorbutic point of view. In such places scurvy may therefore have a room in the discussion concerning the pathogenesis of diseases of the different organs.

Among subjects already dealt with I refer to the question about the relation of scurvy to the infections, p. 120, heart weakness, p. 81, renal calculi, p. 98, liver changes, p. 89. KOSSLER has in 1922 communicated a case where a patient, treated for a digestive disorder with so-called »lenient» dietary, himself out of nervousness limited it still more, whereupon a manifest scurvy set in. Such cases are probably not unfrequent. The question is whether in this case a latent scurvy, caused by the physician, was not already present.[1] Now, earlier authors[2], as well as the present writer, have in scorbutic guinea-pigs stated the presence of ulcers in the ventricle or the duodenum. These ulcers are in the duodenum placed above the papilla Vateri

[1] In the case of CORDIER, reported the same year, medical advice regarding dietary had caused *manifest* scurvy.

[2] The criticism on p. 101, applies to McCarrison's statements in this matter.

and a strong congestive hyperemia is common in this place. One might think of the influence of the acid gastric juice on an atrophic intestinal epithelium, perhaps with a complicating infection. HERZOG presupposes a hemorrhage to be the cause. In any case it is highly important that so-called ulcus-dietary, as well as other »lenient» dietaries, should contain a sufficient dose of antiscorbutic, which surely is often not the case.

It is of the greatest importance to find a test, by which the presence of latent scurvy can be established. Among those indicated for the diagnosis of scurvy by other authors, Roentgen examination of the epiphyses of the long bones, according to FRAENKEL, or of the heart, according to HESS, may be taken into consideration, but these examinations may even in the manifest stage give uncertain results. It seems to me as if the changes in the teeth with atrophy of the processes of the odontoblasts in the dentin, or the precipitate calcium excretion through the urine in the latent stage might be used for creating a method of diagnosing latent scurvy. Experiments in this direction are in progress.

CHAPTER IV.

The calcium metabolism in scurvy.

HESS summarizes the few and partially conflicting examinations of the metabolism in scurvy thus: »The only point in which they agree, is that during the manifest stage the calcium balance is positive.»

Howe and TOVERUD look upon scurvy as a disturbance in the calcium metabolism. Howe writes in 1921: »In calcium disturbances of this kind, two things are to be considered: first, a sufficient supply of calcium and, second, the necessary elements for inducing the fixation of the calcium. The fixation seems to be governed by the vitamine content of the diet.» Thus, Howe and Toverud have a conception of scurvy, which corresponds to that generally prevailing in regard to rickets.

My histological examinations give no reason to suppose that the calcium metabolism is primarily disarranged in scurvy.

On the other hand conclusions may be drawn from the pictures which are highly interesting for explaining the secondary changes which the calcium excretion undergoes in scurvy. In early stages of scurvy a bone is formed which is calcified, but quantitatively as well as qualitatively inferior. The resorption of the old bone seems to proceed normally. The new bone is of small scale and cannot absorb the quantity of calcium made free from the old bone. There ensues in the body a surplus of calcium, and a precipitate excretion takes place, to which the pictures I have found in the kidney in cases of scorbut latens and scorbut mitior bear witness. Afterwards, in the progress of the scurvy a circumstance arises which acts in the opposite direction. Different parenchymatous organs get more and more atrophic and necrotize partially. Dying tissue generally has greater affinity to calcium and thus we see in scorbutic guinea-pigs calcifications appear to a large extent in different organs, principally muscles and liver. This may explain the calcium balance being positive during this stage. In healing, again a strong excretion sets in, which has been noted by several investigators.

This interpretation of the calcium metabolism in scurvy as dependent on different factors has already been sketched in its outlines by GERSTENBERGER. It well agrees with the results gained by LUST and KLOCMANN, BAHRDT and EDELSTEIN, MARIA FRANK (1920).

BAHRDT and EDELSTEIN found considerably diminished calcium and phosphorus contents in bones and muscles of a scorbutic infant. The elements in question were diminished in about the same percentage as the total ash. This discovery is not unexpected where a porotic bone is concerned. Bahrdt and Edelstein are of opinion that it is absolutely contrary to the result of Lust and Klocmann who found a positive calcium balance in florid scurvy, but a negative balance during the healing stage. These apparently opposite results are explicable if we bear in mind that Bahrdt and Edelstein's children had manifest scurvy since at least six weeks back, those of Lust and Klocmann since at least four months.

HOWARD and INGVALDSEN found calcium to be retained during manifest scurvy, but the less, the more the disease proceeded. It is open to doubt, however, whether condensed milk as only diet calls forth simple scurvy in monkey. It is probable that in this food also other necessary substances beside the antiscorbutic are lacking.

MOREL etc. examined the ash and calcium contents in the bones of ten scorbutic guinea-pigs, without further indicating which bones, and stated values fully comparable to those of the control animals. As the calcium contents of the bone *a priori* may be supposed to be diminished in the osteoporotic diaphysis but increased in the epiphysis with its shapeless masses of calcium columns, it is necessary to state clearly from where the examined piece of bone is taken.

PITZ' experiments, like others where no importance has been attached to the quantity of fresh milk consumed, can not be taken into consideration.

ROBB etc. have in 1921 published experiments aimed to elucidate the calcium metabolism in scorbutic guinea-pigs. The arrangement of the experiment with use of calcium-free diet etc. is so unsuitable for the purpose, the judgment of the experimental figures so uncritical, that no notice can be taken of the conclusions.[1]

CHAPTER V.

Scurvy and rickets.

The differences recorded by previous investigators between the bone pictures in scurvy and in rickets have been established by my investigations. Only in one respect, the initial hyperemia, I have found these changes agreeing. Moreover, in scurvy this hyperemia soon gives place in the metaphyses of the long bones to a tissue containing very few vessels, the frame-work marrow. The most pronounced difference between

[1] IWABUCHI found in 1922 no noteworthy changes from the normal of the calcium contents of bones, muscles, liver, spleen, in guinea-pigs with scorbut mitior manifestus, 36—46 days.

scurvy and rickets in the bone-system is their relation to the calcification. In rickets, an osteoid substance is formed, which is not calcified. In scurvy, a bone is formed to a limited extent, which is rapidly calcified. The histological picture gives the differential diagnosis as well as the Roentgen picture (FRAENKEL, HOFFMANN). Already macroscopically, the easily breaking, brittle and light scorbutic bone differs from the flexible, heavy rachitic bone. A real difficulty in distinguishing them only occurs when it is a question of healing rickets. Clinically, a scorbutic and a rachitic rosary may be impossible to distinguish from each other. Other findings will then have to decide the diagnosis.

Through the description, quoted on p. 203, of the bone changes in a child with coincident scurvy and rickets, Quensel has shown how the shares of both diseases in the bone picture may be distinguished, a problem which Schoedel has designated as difficult, if not impossible, to solve.

CHAPTER VI.

Scurvy and inanition.

The question how far the scorbutic changes and symptoms might be consequences of inanition has been examined by several investigators from HOLST and FRÖLICH to COHEN and MENDEL. All of them arrive at a conclusion agreeing with that of the two last-named authors, that »the inanition is a result of the scorbutic symptoms rather than a forerunner of them». The latest to write on this matter are MOURIQUAND and MICHEL: »Le scorbut et l'inanition sont deux faits absolument distincts. Nous estimons que l'apparition des symptômes de scorbut n'a aucun rapport précis avec l'inanition et que cette dernière ne constitue pour eux qu'un épiphénomène généralement tardif.» On the whole the study of my 4 animals, which have been put on relative general inanition but have received a sufficient protective dose of antiscorbutic, has given a concordant result. The animals died after one to two weeks

and showed at the death no trace of the changes of teeth or bones which have been described as scorbutic. In the skeleton muscles, heart, liver, spleen, kidneys, salivary glands, adrenals, of the inanition animals there are light atrophic changes resembling those described in scurvy. It can not be excluded that the inanition has contributed to these changes in certain among the scorbutic animals. In others among these, where there has been no decrease of weight, this is probably excluded. The possible inanition which may have been prevailing during the last days is not sufficient alone to explain these changes in the parenchymatous organs of the scorbutic animals. The difference in degree between the changes in the inanition animals and those with scurvy is too great for that. In the chapter on Pathogenesis I have set forth that I look upon the atrophic changes in animals upon different deficiency diets as similar but not identical.

CHAPTER VII.

A modified method for experimental rating of the antiscorbutic value.

The method for testing the antiscorbutic value of a substance which has up till now been most frequently employed is to determine the minimum protective dose on guinea-pigs. The experimental period has generally been fixed at 90 days, »after which time it is unlikely that death from scurvy will occur» (SHERMAN etc.). MOURIQUAND and MICHEL claim, however, that the animals should live 150 days and more, as they have seen a latent scurvy become manifest as late as that with a constant antiscorbutic dose. Neither the French, nor the American authors say anything about a microscopical examination of the experimental animal.

SHERMAN, LA MER and CAMPBELL point out that if in a certain quantity of a juice, that has been tested with regard to its antiscorbutic value, there is not enough for complete pro-

tection, it is still possible to judge the relative quantity of antiscorbutic administered through comparing the weight curves, survival periods, severity of the symptoms, and autopsy findings for the animals examined with a standard scale. »Thus, one is not confined entirely to a comparison of the so-called minimum protective doses, since the quantitative rating of the degree of protection afforded permits comparisons to be made upon animals receiving less than the amount required for complete protection.» For this a reliable scale of comparison is required. Sherman etc. communicate one. My experiments give another, somewhat different. The origin of the difference is that Sherman etc. do not seem to undertake a microscopic examination in this connection, and thus their minimum protective dose means a dose which protects from changes enough marked to be observed macroscopically at the *post-mortem* examination. As I have proved, a dose twice as large as this is necessary to prevent anatomical changes in the teeth. In my opinion it is to be preferred, by »protective dose» to mean a *fully* protective dose, and in order to establish this amount a histological examination of the teeth is necessary. Of course, the method employed by Sherman etc. is also practicable although somewhat uncertain, if only in every case it is indicated how the experiment has been made.

The early, marked and pathognomonic changes in the teeth of guinea-pigs, which we have described, permit a modification of the indicated methods. After some animals (weight not much above 300 grams) have received a certain quantity of the substance, the antiscorbutic value of which is to be tested, during 2 weeks, they are killed. The lower jaw is decalcified and a cross section of the incisor root is examined in the manner described in the chapter on »Teeth» p. 40. A completely protective dose gives a picture like that in Fig. 30. Smaller doses may to a certain extent be rated by a method analogous to that of Sherman etc., described above, whereby Fig. 22—29 may serve as scale of comparison. *By means of this method, the antiscorbutic value of a product can be tested in three weeks instead of three months.*

CHAPTER VIII.

Pathogenesis of scurvy. Relation of scurvy to other deficiency diseases.

»Viewing the situation broadly, it must be acknowledged that, except for the realization that scurvy is due to a new food factor, a vitamin, our fundamental understanding of its pathogenesis has advanced but little» (Hess 1920). Aschoff and Koch presume »eine kolloid-chemische Umstimmung des Blutes oder der Gefässwände» with »eine fehlende oder schlechte Bildung von Kittsubstanzen, durch deren Mangel die Osteoblasten zur Untätigkeit bestimmt werden und keinen Anreiz zur Neubildung erhalten». From different quarters (Mellanby, Broderich, Taylor, quoted after Orban) the supposition has been brought forth, in accordance with McCarrison's investigation, that the antiscorbutic substance would exercise its influence through the organs of internal secretion. The universal opinion is expressed by Berg 1922 thus: »Wie man die Haupterscheinungen, die wir als teilweise Decomposition bezeichnen könnten, einheitlich aus einem Gesichtspunkte aus erklären soll, bleibt vorläufig ganz rätselhaft».

Two pathogenetic problems have up till now been placed in the foreground for the study of scurvy. The first is this: In which ways does the antiscorbutic influence the osteoblasts and vascular walls, directly or by the means of other organs (glands, endothelial cells)? The second problem is: How does the antiscorbutic exercise its effect, by itself entering the products formed or by rendering certain reactions possible without itself being destroyed?

The present investigation widens the first question. It has been established that the antiscorbutic is necessary to continued activity and life of various more highly differentiated cells in vivid activity, odontoblasts, osteoblasts, chondroblasts, fibroblasts, lymphoblasts, the muscle cells, and the parenchymatous cells of the liver, salivary gland, adrenal and kidney.

All these cells seem, in the absence or deficiency of antiscorbutic, to be subject to atrophy and yield a product which is quantitatively as well as qualitatively inferior. The smaller this insufficient dose of antiscorbutic, the less developed the appearance of these cells and of their products (proved with regard to odontoblasts, osteoblasts and fibroblasts; to be presumed in the rest). If antiscorbutic is altogether lacking in the food, these cells go on living for a certain time and yield during this time products, which deteriorate day by day till the activity is completely arrested and the death of the cell ensues.

HESS says in his chapter on symptomatology: »Scurvy reduces the nutritional state of probably all the cells and tissues of the body.» Even if this is presumable, I would like, in accordance with my investigations, for the time being to formulate this sentence thus: Scurvy reduces the nutritional state and the active function of probably all the most active, most rapidly growing and highest differentiated cells of the body. This reduction begins with the absence of antiscorbutic in the food. It becomes manifest at a rate that varies for the different cells and tissues: first in odontoblasts, then in osteoblasts, muscle cells, lymphoid tissue, fibroblasts, and salivary glands, then in the liver, adrenal, chondroblasts, and last in the epithelium of the kidney. The order in which the changes set in and continue in odontoblasts, osteoblasts and chondroblasts seems to argue for the notion that phylogenetically older and histo-functionally less differentiated cells are later and more lightly struck by the deficiency of antiscorbutic.

The conformity which from a purely histological point of view is found with regard to the cell changes (*cf.*, for instance, hyperemia, the initial disarrangement with disintegration of the gradually lowering cell layer as to odontoblasts and chondroblasts) seems to indicate that antiscorbutic has a similar effect on different cells. It seems to me most probable that this effect is exercised directly on the cells by the antiscorbutic which has passed into the blood. In any case, after my investigation the statement of LUBARSCH still holds true: »Eine

besondere Beteiligung der innersekretorischen Organe bei (der Pathogenese der) Unterernährungskrankheiten ist bisher weder experimentell noch bei Menschen nachgewiesen».

As to the second pathogenetic problem, the inner nature of the influence of antiscorbutic on the cells, my investigation gives no hold. For solving this question special physiological and biochemical experiments are necessary. A few remarks may be made.

ABDERHALDEN and WERTHEIMER have carried out experiments in order to determine the oxygen consumed by different cells under influence of different substances. They also tested various antiscorbutics (juice of lemon, orange, raspberry, maceration of dandelion, sauerkraut, lettuce) and found an increased oxygen consumption in liver, kidney, muscle and lung tissue, and in red blood-corpuscles, but not in brain-tissue, when the above-mentioned antiscorbutics were provided. This effect turned out to be parallel with the antiscorbutic value of those substances so that for instance the acid juices preserved their effectiveness after certain heating, while the neutral and alkaline juices lost theirs, a circumstance which might indicate that we have here to deal with an effect of the antiscorbutic on the oxygen consumption of the cells. — In the same year GYÖRGY published similar investigations with similar result. In this matter, on the other hand, we cannot take into account FREUDENBERG's work (also in 1921), as it seems very uncertain whether the extract of carrots (»Rubio») which he has used has contained any antiscorbutic at all.

The mentioned investigations, connected with the experiences gained of late years (see p. 12) about the injurious effect on antiscorbutic of oxygenation, and my results as to the necessity of antiscorbutic for getting fully satisfactory products of the cellular activity, suggest the possibility that the antiscorbutic is necessary for the oxydative activity of the cells. According to LOEB the cell nucleus is an organ for this activity. In this connection some of my observations are interesting. First, that in the scorbutic atrophy the nuclei from the outset are highly affected and show degenerative changes

(pyknosis). Further, the special form of nucleus change that is represented by the giant-nuclei cells which appear in the muscles in scurvy as well as in inanition.

The question is open whether the antiscorbutic in its effect on cell processes — the nature of which up to the present is altogether unknown — itself enters wholly or partially the newly formed cell products, or whether it is excreted, more or less inactivated.

As the scorbutic changes in the bones are seen most markedly in the growth zones, scurvy has here the same localization as rickets and lues. VIRCHOW says about this question that »alle Organe zur Zeit ihrer physiologischen Kulmination oder gesteigerten physiologischen Funktion am leichtesten Angriffspunkte für äussere Schädlichkeiten darbieten». In the matter of scurvy we must look for a special explanation. Its nature is a diminution even until disappearance of the power of the active cells to renew their respective products, and under such circumstances the changes must be expected to appear first of all in the places where the growth and with that also the resorption are most rapid.

The scorbutic changes have hitherto been defined as a failing apposition in a normally continuing resorption. My investigations modify this definition in two respects. According to these investigations the *inability* of apposition is preceded by a stage where there is a *reduced* ability, which results in a quantitatively and qualitatively inferior product. This product will in the course of the disease more rapidly fall a victim to the destroying powers. There does not seem to be any reason for presuming an increase of these destroying factors, as there are no signs of this in the tissue formed before the onset of scurvy.

The interpretation of scurvy as a general, though not uniform, atrophy of the different tissues and organs of the body agrees well with the clinical symptoms. I have not found any symptom, the scorbutic nature of which is probable, that does

not receive its natural explanation through such an interpretation. Among such symptoms may be mentioned:

1) The sub- or anacidity in the gastric juice (BIERICH);

2) The diminished adrenalin contents in the adrenal (McCARRISON a. o.);

3) The failing regeneration of white and red blood-corpuscles, and their extraordinarily rapid new formation in healing (SALLE and ROSENBERG a. o.);

4) The diminishing of the opsonic index (FORTENATO);

5) The diminished resistance to infections;

6) The appearance of hemorrhages in complications during the convalescence.

This list might be continued to any length. It is of interest to note CRAMER and MOTTRAM's demonstration that certain changes in scurvy — great atrophy of the lymphoid tissue, the thymus, the spleen and the lymphatic glands — can also be brought about through exposure to X-rays.

If the conception of the nature of scurvy which I have arrived at through my studies differs from that prevailing during the last twenty years, yet it does not by any means lack contact with the literature. With regard to the changes in the different organs, this is indicated above in the separate chapters. I will also once more call attention to the statement by HESS, which I have quoted on p. 134. Certain older investigators called their works »De atrophia scorbutico» (MENGERING, 1652). It seems probable that already LINNÉ has observed the calcium deposits in different organs, which have been pointed out by HART and LESSING, then by other authors and are also observed by me. LINNÉ writes in his lectures about 1770: »Thus no materia calculosa arises from fresh fruit. — — — If you go to the butcher's shop in the wintertime, you will certainly see in the animals then killed several signs in liver, heart and lungs of obstructions infallibly arising from dry vegetables which are given them to eat in the winter; but if you go there in the spring and summer when the cattle get green vegetables, you will see that those which are then slaughtered are free from such obstructions».

In order to make clear the relation of scurvy to other deficiency diseases I will dwell upon the appearance of edema in scurvy. Accumulation of liquid in serous cavities and anasarca is often in clinical reports described as a scorbutic symptom. Also in guinea-pigs it is the same, but, as far as I have been able to find, only in cases where the basal diet has not been complete. On the other hand, local edema is often seen in the neighbourhood of large hemorrhages. This edema may be called scorbutic, but it has no *direct* connection with the changes brought about by scurvy in the cells. It is the same with the terminal cardiac edema. NOBEL and WALLGREN, who suppose the presence of an invisible scorbutic edema, attach special importance to the increased quantity of urine, which is found in the beginning of the healing stage. This may be explained, however, without presuming any hidden edema, through the circumstance that when the healing stage sets in, large quantities of dead material from the necrotic tissues are excreted. In any case a scorbutic edema has not yet been proved. Instead it seems probable that the edema present in clinical scurvy ought generally to be placed in connection with the so-called hunger edema (NOEGGERATH etc., IWABUCHI, PRYM, MOURIQUAND etc.). The pathogenesis of this edema has not been made clear. LUBARSCH considers it due to a deficiency of complete albumen, JANSEN a. o. think that the reason is deficient supply of calories with coincident too strong contents of water and salts, other investigators consider vitamin deficiency as an essential factor. It seems certain, however, that the war-edema is caused by deficiency in the food and that it is often clinically found together with other deficiency diseases (beriberi, scurvy).

In the edema disease the main feature of the patho-anatomical picture is an atrophy. It is the same with beriberi, and atrophic features are also seen in other deficiency diseases, as well as in general inanition. Thus several investigators have stated some symptoms to be the same or very nearly the same in beriberi and in scurvy (HESS, DARLING). This is not surprising. STEINITZ and HOPKINS point out that lack of any

substance necessary to a cell leads to the decline and death of the cell, and this applies to the different vitamins as well as to aminoacids and salts. Theoretically, a large number of deficiency diseases are thus to be supposed, besides all intermingling forms, and the symptom which a priori must be expected in these diseases seems to be a more or less general atrophy. That the diseases, which are clinically described as scurvy, beriberi, etc., in reality most frequently are intermingling forms, is probable[1]. Nevertheless, they may each in their simple forms have special pathological features, which the experimental research has to make clear. This investigation, which has just only begun, of the different members in the family of the deficiency diseases, will show the way to a better distinction between them than is now possible. In discussing the different clinical symptoms, also those of scurvy, this undecided state of things must be borne in mind (*e. g.* nyctalopia in scurvy, Loewy 1921). In our Northern countries scurvy may require a special interest among the deficiency diseases, as in its latent forms it is the one most probably met with.

In this treatment of the pathogenesis of scurvy, I have presumed its etiology as established, as being a deficiency in the food of a substance or a group of substances with unknown chemical constitution. However, many German authors have even in recent years kept to the conception of scurvy as an infection or toxic disease. I enter into this question to some extent in my chapter on »Scurvy and infection». These hypotheses — for instance, that of toxic products originating from sterilization of milk — which, to put it mildly, may be termed unnecessary, have been exhaustively reported by NOBEL in 1921. He also dwells at some length upon BOLLE's and BARTENSTEIN's unsuccessful attempts at inducing scurvy in guinea-pigs, but only mentions HOLST and FRÖLICH's work cursorily in two lines, thus giving an example of how national points of view may retard the solving of scientific problems.

The risk involved in an adherence to the theory of infec-

[1] For the cases, described in the literature as »scurvy in breast-fed infants», this is recently proved by POGORSCHELSKY.

tion and neglect of well established investigation results is strikingly demonstrated by the following example. v. PIRQUET indicates in an essay »Die Aufgaben der Küche» 1918 the task of the kitchen to be to prepare quantitatively determined and according to the economical laws selected articles of food so as to make them 1:o innocuous, 2:o digestible, 3:o palatable. For conserving the milk after boiling he recommends hydrogen peroxid. He thus takes no account of the antiscorbutic value of the food. In 1920, CHICK and DALYELL could prove a latent scurvy among the children at the age of 6—14 in v. Pirquet's clinic, owing to the unsuitable preparation of the fresh vegetables, which were given in a fully sufficient ration (200 grams) but were made less valuable as antiscorbutic through the manner of cooking. When this ration had to be reduced to 70 grams, a scurvy epidemic broke out as early as after 8 weeks.

Summary and conclusions of Parts II and III.

The patho-anatomical changes in scurvy have at a closer study been found to be much more widely spread than has been supposed up till now. Such changes have been recognized in all tissues and organs, where the different stages of scurvy were examined. With regard to the bone formation which earlier has been of central interest to investigators, the experiments have established the presence of a hitherto generally neglected stage, before all bone formation ceases. During this stage, which either appears as a period in the development of scurvy, when there is no antiscorbutic in the food, or, with a certain but insufficient dose, represents the definite picture of the disease, the bone-building cells, odontoblasts and osteoblasts, seem to lose more and more of their typical appearance, and the product they yield to diverge more and more from the normal. It seems to be a lowering of dignity, the degree of which is directly determined by the antiscorbutic dose. The characteristics of this scorbutic bone of lower quality, which has been observed by earlier investigators but

generally been misinterpreted, are described for teeth, endosmal and enchondral bone formation. For the connective tissue a general atrophy is described, which especially overtakes the collagen fibrils. This change is also proved in the vascular walls. In muscles, lymphoid tissue, liver, salivary gland, adrenal and kidney an atrophy combined with necrosis has been found. Also in these regions the tissues seem more severely struck, the more the scurvy is developed. It is established that some of the most active and most differentiated of the cells in the body are caught earliest and most severely by the scorbutic atrophy. The changes which have been described may be traced at a very early stage of the latent period. The importance of subjecting this latent stage to a close study is strongly emphasized.

Through these investigations the pathological picture of scurvy has thus been amplified, and the principal features of the disease have been analysed and found to be uniformly explainable.

PART IV.

Scurvy and tuberculosis.

CHAPTER I.

Historical review.

An importance of the diet to the progress of tuberculosis has been assumed already by Linné. He writes in 1766: »Ingesta nimis nutrantia — nonne hinc saepissime oritur Phtisis juvenum?» On the contrary, subsequent investigators have as a rule regarded the general malnutrition as acting upon the progress of tuberculosis, though the problem up till the present time has evoked a comparatively small interest. Cornet and Kossel write in 1913: »Es ist wohl denkbar, dass ein abgekapselter Herd durch Unterernährung ausgelaugt und die Bacillen mobilisiert werden». The authors are evidently thinking of the theory of »demineralisation». Löwenstein, who in the

same textbook (KOLLE-WASSERMANN) writes the chapter on »Tuberkuloseimmunität», is briefer still. In the first volume of BRAUER-SCHRÖDER-BLUMENFELD'S »Handbuch der Tuberkulose», 1915, HANS MUCH writes a hundred pages about »Die Immunität», without mentioning the influence of the food. FRIEDRICH MADSEN writes in the same volume about »Disposition und individuelle Prophylaxe». He mentions the malnutrition only in passing and ends with some rules for the prophylaxis, which apply to the community and to the individual. The public measures include neutralizing of expectoration, hygien of the infants' milk, settling of the housing problem, sanatorium treatment for the severest cases, compulsary notification for the arranging of home disinfection and hospital nursing. The individual prophylactic measures are summarized thus:

»1. Belehrung der Einzelnen über Infektionsgefahr.
2. Erziehung zur Reinlichkeit.
3. Abhältung der minder Widerstandsfähigen von besonders gefährdeten Berufen.
4. Kräftigung aller durch Hygiene der Schule, Erziehung zum vernünftigen Sport u. s. w.»

What the author wishes to set forth with regard to the choice of suitable food will thus lie contained in the »u. s. w.» — No more does PHILIP (1922), apart from the zomotherapy, mention anything about the relation of different articles of food to tuberculosis.

Most of the systematic experiments on the subject that have been undertaken are devoted to this so-called zomotherapy. It originates in experiments by HÉRICOURT and RICHET (1900). These investigators found in the case of dogs inoculated with tuberculosis that a good effect was worked through injecting juice from raw meat. The zomotherapy consists in feeding through the mouth with larger or smaller quantities of juice pressed from raw meat. It has been praised by many (RAISONNIER, JOSIAS, JOSIAS and ROUX, PHILIP), by others not (STEINITZ and WEIGERT). It does not seem to have been made much use of. Without entering into the question it

may only be pointed out, that all those who advocate it, indicate that the meat juice is effective only when raw. In this connection I may remark that BARLOW recommended raw meat juice as a good antiscorbutic in infantile scurvy.

Here I would like to mention in a few words an experiment which was made by me in the children's hospital »Samariten»[1] during the winter of 1916—1917. Twenty children of different ages with different kinds of tuberculosis, most of them with tuberculosis of the bronchial glands, were given a daily dose of 50—100 ccm. of raw blood serum each. The blood was gathered under certain precautions at the daily slaughtering of cattle in the slaughter-house of Stockholm and was placed in the freezing-room. The serum was taken up by pipet the following day and given to the children in cocoa. It was taken readily. The experiment went on for four months. The effect on the children's state of health seemed striking. Their appetite, colour and tonus improved, and the tuberculous process went rapidly towards healing, as far as could be judged clinically and by Roentgen rays. However, only a small number of the children remained in the hospital during the whole period of the experiment, and there was not a sufficient number of control patients, wherefore the experiment can not be said to have been conclusive.

Other experiments are few. In 1907, R. WEIGERT made experiments with different feeding of pigs infected with tuberculosis. These experiments are said to have shown that the animals fed on a diet rich in fat (whole milk and oil of sesame) resisted the tuberculosis better than those fed chiefly on carbohydrates (buttermilk and bran, potatoes). First of all the general condition was better, and then there was also a certain difference in the extent of the process. But the diets used differ also in other respects than fat and carbohydrates. The fat-rich diet must especially have held more A-vitamin. The experiments of THOMAS in 1913 only comprised 6 animals and gave ambiguous results. KARCZAG states

[1] Chief: Dr. R. NORDGREN, to whom my thanks are due for his kind assistance in the experiment.

in 1919, that his attempts to act on the tuberculosis allergy gave the same results in man and in guinea-pig. The two most important factors are light and abundant nutrition. The changes in the allergy, however, were not at all parallel with the progress of the tuberculosis. Albinoes, for instance, showed better allergy but succumbed sooner to death.

GERHARTZ undertook in 1922 experiments as to the influence of age on the progress of tuberculosis in guinea-pigs. He arrives at the conclusion that »es kann kein Zweifel bestehen, dass sich tierexperimentell eine Abhängigkeit der Tuberkulosekrankheitsdauer von Ernährungszustand und Alter des Tieres zur Zeit der Infektion auch bei exakter Anordnung des Versuches nicht erweisen lässt». What is proved by Gerhartz' experiments is that with a dosage of infection calculated per 100 grams and with uniform dietary (we are not told which), the progress of guinea-pig tuberculosis is very heterogeneous, and that the differences seem independent of the age of the animals.

The increased spread of tuberculosis in Germany during and after the World War has stimulated the interest in that country in the question of a conjunction between food and tuberculosis. So far, however, the statements diverge.

W. STOELTZNER writes in 1920: »Dass die Tuberkulose seit dem Kriege bei uns in erschreckender Weise an Zahl und an Schwere zugenommen hat, ist allgemein bekannt. Ebenso ist wohl nicht daran zu zweifeln, dass die Kriegskost die wichtigste Ursache dessen ist. Ist nun das schädliche in der Kriegskost die quantitative Unterernährung oder ihre qualitative Eigenart?» On the ground of clinical experiences Stoeltzner answers the question thus: »Wahrscheinlich trägt das einseitige Vorwiegen der Kohlehydrate in der Kriegskost die Hauptschulde an dem Überhandnehmen der Tuberkulose».

KIEFER says in 1922: »Alle die schönen Theorien über Disposition und Immunität, müssen nach den grossen Experimenten des Krieges, der Blockade, der Armut, gründlich revidiert werden». He states that the tuberculosis in Germany has increased and assumed a more malignant character. Among

circumstances that determine the prognosis he mentions »die deletären Folgen der langdauernden Unterernährung»; among predisposing illnesses several, but not scurvy.

In Aschoff's large »Handbuch der ärztlichen Erfahrungen im Weltkriege», vol. VIII, Weinert writes about »phtisische Infektionen». He mentions various circumstances that may aggravate the progress of tuberculosis, even »Schussverletzungen», but does not mention scurvy. No more does Beitzke, who in the same handbook writes about »fortschreitende Phtisen». Nor does Aschoff himself seem to have thought of any relation of cause and effect, when in his book »Skorbut, von L. Aschoff und W. Koch», 1919, he says that among a material of 23 soldiers, dead of scurvy, he had found the majority (the number is not given) suffering from florid tuberculosis of different kinds: »Tuberkulose der serösen Höhlen, der Meningen, Miliartuberkulose, Lungen- und Darmphtise.» Aschoff and Koch wish to see an explanation of this in the fact that the majority of the patients were Turks, in whom they assume a special predisposition for tuberculosis.

Selter und Nehring, on the other hand, in 1921 subjected to a closer analysis the relation between the food and the increase of the tuberculosis death rate in Germany during the war — chiefly on account of the change in the curve for the tuberculosis death rate during the war in German towns with more than 30,000 inhabitants. The apex of the curve, instead of lying as otherwise in April, was during the years 1917—1919 advanced till May. From the interesting account I quote the following:

»Die Verschiebung nach dem Sommer hin spricht nicht dafür, dass klimatische Faktoren den allein entscheidenden Einfluss auf die Tuberkulosesterblichkeit haben. Ganz unerklärlich wäre dann auch die noch weitere Verschiebung von vier Wochen, auf Mitte Mai, in den Jahren 1917—1919, wo die Tuberkulösen, durch die Unterernährung geschwächt, eine erheblich geringere Widerstandsfähigkeit hätten haben müssen und infolgedessen die Höhepunkt der Sterblichkeit gerade in diesen Jahren früher zu erwarten gewesen wäre. Der monatliche Verlauf der Tuberku-

losesterblichkeitskurve scheint uns darauf hinzudeuten, dass neben den Witterungsverhältnissen im Winter und den dadurch bedingten Erkältungskrankheiten auch die Ernährung, die bekanntlich im Winter vom Monat zu Monat qualitativ schlechter wird, da sie, wenigstens bezüglich der Kohlehydrate immer mehr auf eingekellerte und konservierte Nahrungsmittel angewiesen ist, eine grosse Rolle spielt. *Man könnte an die Vitamine denken*[1], die für den Tuberkulösen vielleicht besonders wirkungsvoll sind. Im Beginn des Sommers, sobald die Zufuhr des frischen Gemüses einsetzt, sinkt die Sterblichkeit, erreicht im Herbst ihren tiefsten Stand und bleibt in den Friedensjahren (1914 und 1920) auch im ersten Teil des Winters auf einer niedrigen Stufe. Hierdurch könnte vielleicht auch die auffallende Verschiebung der Gipfel in den Jahren 1917—1919 erklärt werden, da durch die Gemeinbewirtschaftung und teilweise Rationierung der Gemüse die Versorgung der Bevölkerung hiermit erschwert und verzögert wurde.

Eine ausreichende Ernährung dient nicht nur dazu, den einzelnen Menschen wieder voll arbeits- und leistungsfähig zu machen, sie wird auch das wirksamste Mittel zur Bekämpfung der Tuberkulose sein.

Unter den sozialen Faktoren, welche auf die Tuberkulosesterblichkeit von Einfluss sind, sind zweifellos die Ernährungsverhältnisse am wichtigsten, wichtiger als die Wohnungsverhältnisse.»

A statement by KAISERLING to the same effect is quoted by ADAMS and HAMILTON:

»That the increased rate of tuberculosis (1917 and 1918) is due to food and not to other incidents of war, is shown by the slight rise before the tightening of the blockade and the rapid rise after it. German physicians are beginning to say, that tuberculosis should be regarded primarily not as an infectious disease but as a disease of nutrition, to be controlled much more by feeding than by preventing infection — —.»

ADAMS and HAMILTON add:

»In the wards for tubercular children we saw varieties of the disease which used to be regarded as medical curiosities, so extreme as to be seen only in primitive people with no racial immunity. Germany's racial immunity, if there really be such a thing, was destroyed by the blockade.»

[1] The italics are mine.

Remarkable is also GEOGHEGAN's description from the West Indies. On the whole these islands have a rich vegetation, a relative prosperity and a varied diet. The climate is excellent. One group of islands, however, the Turk Islands, are conspicuous for the poverty of the inhabitants. Their food is as a whole limited in variety, inferior in nature, and deficient in freshness. Starchy foods predominate. While tuberculosis as a rule is but little spread in the West-Indian archipelago, the Turk Islands have a predominance of tuberculosis.

In his excellent monography on scurvy, of 1920, which has been frequently quoted above, HESS writes, p. 88: »Active tuberculosis is a not uncommon secondary manifestation», and p. 99: »Tuberculous lesions are also frequently present, and are stated to assume fresh activity as the result of the nutritional disorder.»

The best support for such a supposition is given by the material of scorbutic patients, over which SALLE and ROSENBERG report in 1921. In different groups the figures for complicating tuberculosis were 9—22 %. All their deaths were due to tuberculosis, often in its miliar form. Out of 461 cases of scurvy, 17 died, that is, 3.6 per cent. Salle and Rosenberg speak with great assuredness of the mutual relation between scurvy and tuberculosis:

»Wenn somit die Tuberkulose einer Skorbutentwickelung die Wege ebnet, so bedeutet andererseits das Hinzutreten von Skorbut zur Tuberkulose häufig eine sehr ernst zu nehmende Komplikation. Wir erwähnten schon, dass bei unseren sämtlichen Todesfällen Tuberkulose die Todesursache war. Wie diese deletäre Wechselwirkung zu deuten ist, ist unklar. Klinisch war bei einer grossen Anzahl der Fälle der progrediente unaufhaltsam zum Tode führende Charakter der Tuberkulose ebenso auffallend, wie die häufig schlechte Beeinflussbarkeit skorbutischer Symptome durch sonst sicher wirkende diätetische Massnahmen.»

It can not but strike us, how many of the more closely examined cases of infantile scurvy have been complicated by a florid tuberculosis. Thus it was, for instance, in three of SCHOEDEL's five cases, one of INGIER's three, in SCHMORL's and NAEGELI's children and one of HART and LESSING's five monkeys.

As to the question, on the other hand, about the influence of tuberculosis on the onset of scurvy, BIERICH gives a negative verdict. He founds this on a very large material, 1,343 cases of scurvy patients, of whom more than 10 per cent. were tubercular. He says briefly that the tuberculosis does not seem to have had any predisposing influence on the onset of scurvy.

These statements and experiences of a connection between tuberculosis and scurvy, or a lack of fresh vegetables, are of the very greatest interest. A factor which somewhat lessens their cogency is, that persons who die of scurvy often also (see p. 139) have suffered from the want of other substances than the antiscorbutic. A-vitamin will often have been lacking in the food, which will probably also in other respects have been insufficient.

In the literature I have found but one attempt at experimentally elucidating the question of scurvy and tuberculosis. MOURIQUAND and MICHEL, who in 1921 state that they have found the injection of thyroid extract to turn a latent scurvy into manifest, mention in a note that one of them together with a deceased physician, Ménard, has occupied himself with experiments in order to find out whether tuberculosis might have a similar influence.[1]

In 1920 I pointed out the high A-vitamin contents of the cod-liver oil and the dairy products as a possible explanation of the high esteem in which of old they are held in the tuberculosis therapy, compared to other fats. The relation of A-vitamin to tuberculosis, as a matter of fact, is also well worth experimental testing.[2] In the course of my experiments I

[1] MOURIQUAND, MICHEL and BERTOYE in 1922 published the negative results. They gave also a preliminary note of experiments aimed to elucidate the influence of scurvy on the progress of tuberculosis. The experiments had not given conclusive results.

[2] Already in 1907, WELLS will have seen a favourable effect on the tuberculosis in pigs of feeding with cod-liver oil. HAPP and WAGNER studied 1923 the question clinically in infants and KASSOWITZ in elder children, without conclusive results. For the present, M. SMITH is engaged in such experiments on guinea-pigs, of which he in 1923 gave a first communication.

have subjected the C-vitamin to such testing. I have gone along two lines. First I have tried to investigate the mutual relation of scurvy and tuberculosis in guinea-pigs. Then I have also attempted clinically to test the influence of the antiscorbutic on the progress of tuberculosis in man. The latter investigation, however, is chiefly to be looked upon as a preliminary of future research on a larger scale.

CHAPTER II.

Experimental studies on guinea-pig.

Technique and survey of experiment.

(Records of cases see p. 206.)

The experiment was carried out between March 29th and July 3rd, 1923. 86 guinea-pigs were used for the purpose; 62 of them were bought from a private breeder in the first half of February at the age of two weeks and were fed by me on complete dietary (cereal, bran, milk, swedes) for more than seven weeks. The remaining 26 were bought on March 17th from an institution and were fed nearly two weeks on complete dietary by me, as they had earlier been in the institution. The first weighing of the animals was undertaken March 19th and 20th.

WALLGREN, after experiments on rabbits, is very exacting with regard to the choice of animals for tuberculosis experiments. He claims that they should all be of the same age and preferably of the same litter. As for guinea-pigs, however, GERHARTZ has not been able to demonstrate any influence of different ages on the progress of tuberculosis. The lifetime after the injection of a certain dosage of tubercle bacilli is very different for these animals, and the same thing applies to animals of the same litter that have the same dietary. This ought to be borne in mind when judging the experiments. But it does not by any means prevent the use of guinea-pigs as experimental animals in tuberculosis experiments as long as the results are judged with due discrimination.

Half the number of experimental animals were infected on March 29th, 1923, with the same dosage of tubercle bacilli, 0.00005 gram. The bacilli were obtained in a homogeneous emulsion from the Public Medical Institute. They were of its stock No. 80, human type, indicated of low virulence, and came from a culture a fortnight old. The injection was made intramuscularly into the adductors on the inner posterior side of the right thigh. During the first twenty-four hours after the injection the animals were somewhat dishevelled and felt hot. After another twenty-four hours, they could not be distinguished from the controls as far as appearance and liveliness went.

GRÜNER and HAMBURGER indicate a somewhat lower dosage of tubercle bacilli (0.000005 gram) as a suitable dosage of infection in experimental studies on guinea-pigs, and JOEST and EMHOFF have used a still smaller dosage (0.000001 gram).[1] In order to determine a suitable dosage of stock No. 80, I made a preliminary experiment, seven animals (No. 13—19) having been injected with doses on a sinking scale from 0.0025 to 0.0000005 gram. According to the outcome of this experiment the dosage was fixed to 0.00005 gram.

The animals were divided into groups, with 8 (7) animals in each, the groups receiving different dietary from the day of injection. In each group half the number were tubercularly infected. Yet the animals on complete dietary of cereal, bran, 60 ccm. of unboiled milk and fresh swedes, were 16 in number, of which 8 were tubercularly infected. 8 of the animals had scorbutic diet (see p. 12). The remaining 65 had the same scorbutogenetic basal diet and besides different doses of preserved orange juice. This latter I had prepared immediately before the experiment by pressing the juice of fresh juicy oranges, pouring it into smaller bottles of 200 grams, which were warmed, stoppered and boiled during 30 minutes immersed in water. The dosage of the juice and the grouping of the animals are shown in detail by Table 6. Since the experiment indicated that the minimum protective dose

[1] M. SMITH used a larger dose (0,0005 gram).

Table 6.

Division of guinea-pigs within different groups.

Dietary per day and animal.	Fraction of m. pr. d. of antiscorbutic	Numbers of *animals not* infected with *tuberculosis*	Numbers of *animals infected* with *tuberculosis*
Complete mixed dietary	More than 1.0	97. 98. 99. 100.	104. 105. 106. 107.
		101. 102. 103. 183	108. 109. 110. 111
Scurvy dietary = Sc.	0	112. 113. 114. 115	116. 117. 118. 119
Sc + 0.3 ccm. pres. orange juice	0.1	120. 121. 122. 123	124. 125. 126. 127
Sc. + 0.6 » » »	0.2	128. 129. 130. 131	132. 133. 134
» + 1.0 » » »	0.3	135. 136. 137. 138	139. 140. 141. 142
» + 1.5 » » »	0.5	143. 144. 145. 146	147. 148. 149. 150
» + 2.0 » » »	0.7	151. 152. 153. 154	155. 156. 157. 158
» + 2.5 » » »	0.8	159. 160. 161. 162	163. 164. 165. 166
» + 3.5 » » »	More than 1.0	167. 168. 169. 170	171. 172. 173. 174
» + 5.0 » » »	More than 1.0	175. 176. 177. 178	180. 181. 182
		179	

(m. pr. d.) of this juice was larger than 2.5 ccm. and smaller than 3.5 ccm., it has been approximately fixed at 3 ccm., and the quantity of antiscorbutic given to each group has been calculated accordingly as fraction of the minimum protective dose. The inaccuracy involved in this estimating of the m. pr. d. may be put to $\pm$ 0.5 ccm. = 17 %. This relative figure is also applicable to the fractions of the m. pr. d. With the uncertainty which is still incident to the upper limit of the range of scurvy (see p. 126) the most important thing, however, is not the absolute figure, but the relative value of the doses in the different groups.

The tubercular animals that died during the course of the experiment or were chloroformed at the conclusion after ninety odd days, in all 42, were examined macro- and microscopically. For determining the degree of scurvy, teeth and ribs were

Table 7.

Survey of experiments.

Abbreviations and terms the same as in the table on p. 18.

Series	Number	Diet	Weight in grams		Scurvy	Infected with tbc	Lifetime days	Remarks
			initial	final				
	97	Complete dietary	165	250	0	0	52	Died of bronchopneumonia ac.
XXIV	98		150	460	0	0	96	Killed
	99		245	545	0	0	96	»
	100		230	560	0	0	96	»
	101		160	445	0	0	96	»
	102		130	575	0	0	96	»
	103		200	515	0	0	96	»
XXV	104		150	665	0	*	93	»
	105		300	560	0	*	93	»
	106		200	570	0	*	93	»
	107		180	210	0	*	29	
	108		290	490	0	*	93	Killed
	109		250	540	0	*	93	»
	110		260	550	0	*	93	»
	111		290	430	0	*	70	
	112	Basal scorbutic diet = sc.	390	235	****	0	28	
	113		390	260	(****)	0	19	
	114		410	410—	****	0	1	
XXVI	115		390	260	****	0	29	
	116		445	360	****	*	18	
	117		545	335	****	*	33	
	118		495	390	****	*	36	
	119		470	280	****	*	24	
	120	Sc. + 0.1 m. pr. d.	370	270	***	0	15	
XXVII	121		375	280	***	0	25	Drowned in the milk basin
	122		390	230	***	0	42	
	123		360	210	***	0	32	

Series	Number	Diet	Weight in grams: initial	Weight in grams: final	Scurvy	Infected with tbc	Lifetime days	Remarks
XXVIII	124	Sc. + 0.1 m. pr. d.	460	270	***	*	23	
	125		425	310	***	*	58	Died of pneumonia ac.
	126		425	315	***	*	43	
	127		410	28	***	*	17	Died of pneumonia ac.
	128	Sc. + 0.2 m. pr. d.	405	270	**	0	15	Colitis ac.
	129		390	310	**	0	22	Gastroduodenit. ac.
	130		370	290–	**	0	29	
	131		370	290	***	0	21	
	132		450	270	***	*	43	
	133		440	330	***	*	86	
	134		410	350–	**	*	6	Died of pneumonia + necrosis ac. pancreat.
XXIX	135	Sc. + 0.3 m. pr. d.	415	360	**	0	83	Abscessus lienis ruptura et hepatis
	136		425	370–	**	0	64	
	137		385	265–	**	0	37	
	138		270	285	**	0	40	
	139		460	480	**	*	77	Died of ruptura lienis
	140		395	320–	**	*	43	
	141		360	350–	**	*	52	
	142		375	275	**	*	76	
XXX	143	Sc. + 0.5 m. pr. d.	340	245	**	0	59	Died of septicemia
	144		395	540	*	0	92	Killed
	145		370	230	*	0	18	
	146		270	395	*	0	92	Killed
	147		430	295	*	*	32	
	148		380	340	**	*	56	
	149		425	380	**	*	92	Killed
	150		395	265	*	*	28	
XXXI	151	Sc. + 0.7 m. pr. d.	355	500	*	0	92	Killed
	152		270	250	*	0	22	
	153		375	420	*	0	90	Died of pleuropneumonia
	154		310	280–	*	0	6	
	155		410	280	*	*	19	Ulcus duodeni
	156		405	435	*	*	92	Killed

Series	Number	Diet	Weight in grams initial	Weight in grams final	Scurvy	Infected with tbc	Lifetime days	Remarks
XXXI	157	Se + 0.7 m. pr. d.	355	265	*	*	22	
	158		312	210	*	*	40	
XXXII	159	Se + 0.8 m. pr. d.	345	275	*	0	29	Died of gastroenterocolitis ac.
	160		350	580	*	0	92	Killed
	161		325	520	*	0	92	»
	162		355	520	*	0	92	»
	163		270	280	*	*	11	
	164		410	325	*	*	44	
	165		410	410	*	*	90	
	166		295	210	*	*	89	
XXXIII	167	Se + 1.2 m. pr. d.	315	220	0	0	12	Died of appendicitis ac.
	168		325	475	0	0	93	Killed
	169		290	440	0	0	93	»
	170		335	470	0	0	93	»
	171		365	445	0	*	93	»
	172		325	340	0	*	24	Died of pneumonia ac.
	173		350	430	0	*	89	Ruptura lienis
	174		280	230	0	*	42	
XXXIV	175	Se + 1.7 m. pr. d.	150	145	0	0	17	
	176		155	240	0	0	75	Pneumonia, peritonit. ac.
	177		180	215	0	0	28	Bronchopneumonia
	178		250	620	0	0	93	Killed
	179		240	440	0	*	93	» , pneumonia ac.
	180		290	310	0	*	38	Died of » »
	181		200	450	0	*	93	Killed
	182		265	380	0	*	93	»
XXXV	183	Complete dietary	330	515—	0	0	96	Killed. Had for some time beriberi-like symptoms
	184	40 gr. wheat + 6 ccm. orange juice, 2.0 m. pr. d.	380	270	0	0	8	
	185		235	150	0	0	14	
	186		300	200	0	0	11	
	187		250	160	0	0	7	
	188	Complete dietary	280	280	0	0	11	Killed
	189		340	340	0	0	1	»

principally examined. For the study of the tuberculosis, the attention was chiefly directed to the local focus in the thigh musculature, regional lymph-glands, spleen and liver. The other organs were examined microscopically as far as the macroscopical examination gave reason for supposing changes within them. Lungs and lymph-glands other than the regional ones have thus been examined in most cases. Six local foci in the thigh musculature (No. 119, 125, 126, 127, 155, 171) are not noted in the records of the macroscopic examination. One of these (Case 171), was found in series of sections at microscopical examination, whereas in three (Cases 119, 127 and 155), pictures were had from the immediate vicinity of the necrosis. Microscopic pictures are lacking from the primary focus in Cases 106, 148. For the regional lymph-glands microscopical examination is lacking in 6 cases, No. 107, 116, 134, 139, 155, 166; for the spleen in one case, No. 157. The reason for this incompleteness of the microscopical examination, which, however, is of no very great importance to the study, the material being so large, was a misunderstanding between the author and the technical aid. The number of the examined sections also for this latter part of the examination still is greater than 1,500. They have been stained in three ways, all with hematoxylin-eosin, the majority also with Hansen's connective-tissue stain, and with Ziehl's carbol-fuchsin on tubercle bacilli. For specific cases other special staining methods, mentioned on p. 32, have been used.

Influence of scurvy on tuberculosis.

Progress of the tuberculosis.

The weight charts are found on pp. 207—233. They show that in general the curves of the tubercular animals follow those of the control animals, the lifetime seeming in most cases to be determined by the antiscorbutic dose. Series 32 is an exception (daily dose 0.8 m. pr. d.), p. 225, in which series three of the controls were alive at the conclusion of the experiment, but none of the tubercular animals. One of these died of general tuberculosis on the 90th day after the injection.

Out of the 15 tuberculized animals that had an antiscorbutic dose large enough to protect them from all scorbutic pathological changes (Series 25, 33 and 34), 9 animals, or 60 %, were alive at the conclusion of the experiment after 93 days. Out of 16 animals not infected, 12, or 75 %, were alive. The death rate for the tubercular animals was thus a little higher. Two of these dead animals had general tuberculosis (No. 174 after 42 days, No. 111 after 70 days). In one case (No. 173, 89 days) the cause of death was rupture of the spleen, which was changed tubercularly.

The progress of the tuberculosis was fairly uniform. Thus, 24 of the 25 animals that lived more than 40 days showed tuberculous changes, besides locally in the muscle, in the regional glands, spleen and liver, also in one or more other organs. One animal on complete dietary, No. 171, showed no clinical symptoms of tuberculosis, and no macroscopic changes when killed after three months. In series of sections from the thigh musculature the miliary primary focus was found, fibrously healed; no tubercle bacilli were demonstrable.

Among the animals that died during the first 40 days of the experiment, the extent of the tuberculosis was more heterogeneous, as is seen from Table 8.

Table 8.

The extent of tuberculosis in animals, dead after a different number of days since beginning of experiment, having had different doses of antiscorbutic, counted in ccm. of preserved orange juice, and in fractions of m. pr. d. The numbers are those of the animals in the Records.

Abbreviations:

l o = *tuberculosis* found in the place of injection in the thigh musculature and in regional lymph-glands;

l i = besides in the primary focus also in the spleen;

h = besides in the primary focus also in the liver;

u = tbc found also in other places than the primary focus, liver and spleen.

Dietary	Fraction of m. pr. d. anti-scorbutic	Days		
		10—20	20—30	30—40
Sc = scorbutic diet . . .	0	116 u	119 u	117 li h 118 u
» + 0.3 ccm pres. or. j	0.1	127 li	124 u	—
» + 1.5 » » » »	0.5	—	150 u	147 u
» + 2 » » » »	0.7	155 o	157 lo	—
» + 2.5 » » » »	0.8	163 u	—	—
» + 3.5 » » » »	>1.0	—	172 u	—
» + 5 » » » »	>1.0	—	—	180 li h
Complete dietary . . .	>1.0	—	107 o	—

It is seen from the Records that the number of microscopically examined organs is not the same for the different animals, and also that this can not explain the differences noted. That the different progress can no more be explained as owing to the different degree of scurvy, is also immediately evident from the table. Yet it is remarkable that the tuberculosis in the animals with pure scurvy dietary showed a larger extent than in many of the rest, and also that among these four animals suffering from scorbut gravior there was one, No. 118, where already after 36 days caseous glands were found in the hilus of liver and lung, a change not seen in any of the other ten animals.

A similar difference in the extent of tuberculosis in guinea-pigs is found by Gerhartz, who no more than the present writer considered that it could be explained by the different age or sex of the animals. In my experiments the C-vitamin has been varied without conclusive effect. Possibly a more distinct result would have been gained if a smaller dose of tubercle bacilli had been injected. The supply of A-vitamin has been practically constant. Among the factors that may have varied in my experiments, I mention:

1) the hereditary conditions of the animals;

2) the dietary of the mother during pregnancy and suckling;

3) other conditions during the first weeks;

4) the place of the injection of tubercle bacilli (more or less superficially; into or between muscular bundles; with or without opening blood or lymph vessels);

5) the pressure at the injection;

6) intercurrent acute infections, not always easy to diagnose.

Character of the tuberculous changes.

The changes found in the 15 animals that had a complete dose of antiscorbutic agree with those described by earlier writers. The primary focus in the musculature was bounded by a rind of connective tissue more than a millimeter thick. It was also penetrated by connective tissue. This connective tissue was seen also at the microscopical examination to penetrate with its extraordinarily strong collagen fibrils the necrotic primary focus in the musculature (Plate III) as well as other tuberculous foci (Plate V). Near the primary focus there were seen muscle fibres, parts of which were necrotized and to a large extent calcified. There was also an increase of fibroblasts. Also in the primary focus itself as well as in the regional lymph-glands and often in the spleen, extensive calcifications are seen. This finding is different to that of RÖMER who in his large material only saw two guinea-pigs with calcification of tuberculous foci. The extensive calcification may perhaps be placed in connection with the small virulence in our stock of bacilli. In Case 104, typical Langhans' giant cells were seen in the primary muscle focus, the protoplasm of which was for the greater part calcified. About the genesis of these cells there has been disputes. The abovementioned observation I interpret as favouring the conception that these giant cells are results of a beginning degeneration (BAUMGARTEN a. o.). The pictures do not give the impression of a calcium lump absorbed by the giant cell from the outside, but of a diffuse calcification of the protoplasm of the cell.

In spleen and liver there was typical tuberculous granulation tissue, but of different character; necroses, as has already earlier been described by others, dominating in the spleen

picture, and a cirrhosis in the liver picture. In the spleen the tubercle bacilli were more numerous than in the liver, but also in each liver with an incipient cirrhosis bacilli were found, with some few exceptions, already in the first or second preparation. At such a change in the liver which may justly be called a cirrhosis tuberculosa, there are seen regenerative strands of young liver columns, fibroblasts with cells of different types, epithelioid cells and giant cells, part irregular, part of Langhans' type. It has earlier been described in guinea-pigs by STOERK, and afterwards by GOUGEROT, KLING and LICHTENSTEIN. It is of the greatest interest to note this constant reaction of the guinea-pig liver to slight tubercular infection, especially in view of the elucidation it may give to certain liver cirrhoses in children with slight tubercular infection (older writers, reported by Höjer). It was a striking circumstance that in the tuberculous foci, besides typical Langhans' giant-cells, there were also often found atypical such cells, and among them many that were more like the type described by STERNBERG. Since in my material tubercle bacilli of a not very virulent stock were injected, possibly (LICHTENSTEIN) pictures like those in lymphogranulomatosis STERNBERG—PALTAUF might be expected. A great number of the lymph-glands were uniformly swelled without macroscopically visible foci, but at the microscopical examination epithelioid cells and tubercle bacilli were found in them. Neither the macroscopic nor the microscopic picture otherwise resembled that shown in Sternberg's lymphogranulomatosis. In the granulation tissue no eosinophile cells or »mast-cells» were found, nor were any plasm-cells found by staining according to Pappenheim.

At the macroscopical examination of the tubercular animals that had severe scurvy, an essential difference from the picture just described was at once conspicuous. The tuberculous foci in muscle, lymph-gland or spleen were not seen to be surrounded or penetrated by any connective tissue (Plates IV and VI). The necrotic parts passed without such demarcation into non-tubercular tissue. Besides this lack of reactive tissue, where such might be expected, there were found, together with the par-

enchymatous atrophy of the organs in question, also the atrophy already described of the connective tissue, present before the onset of scurvy in muscle tendons, trabeculae of lymph-glands and spleen, vessels, etc. The material was stained, for the microscopical examination, with hematoxylin-eosin through which the cell form appears distinctly, and also to a large extent according to Hansen with trioxihematin for the study of the collagen tissue. In both series these changes were marked. They both showed that in the animals standing between those purely scorbutic and those fed on full dietary the connective tissue had a different character, which more or less approached the two extremes according to the scorbutic dose given to the animal. The result of the examination of the preparations is found in Table 9.

In this table the development of the connective tissue is indicated in five degrees, by C 0—C 4, thus:

C 0: no connective tissue reaction around or within the tuberculous foci. Especially there are no collagen fibrils in cells which might be interpreted as fibroblasts. At the same time there is in the old connective tissue a specially pronounced atrophy of the collagen substance.

C 1: thin layers and strands of fibroblasts appear. These fibroblasts seem to form collagen substance, though not in long fibrils but like a lump near the nucleus or an irregular ball of short threads. The cells do not seem placed in any marked order.

C 2: pronounced tendency to a parallelism between the cells mentioned. For the rest like C 1.

C 3: the fibroblasts have normal appearance, are arranged as in normal cases around and in the tuberculous foci, and form elongated collagen fibrils. The connective tissue is tender, however, both macro- and microscopically.

C 4: strong, rindlike, normal connective tissue with strong collagen fibrils in and about the tuberculous foci. No

Table 9.

The degree of fibrous reaction of the connective tissue in and around tuberculous foci in animals, dead a different number of days after beginning of experiment, and given different doses of antiscorbutic, counted as fraction of minimum protective dose (m. pr. d.). This dose is fixed at 3 ccm. of the orange juice used (see p. 151). The numbers are those in the Records, p. 206. The strength of the reaction is expressed in 5 degrees (C 0—C 4), explained p. 161.

Fraction of m. pr. d. antiscorb.	Number of days from beginning of experiment till death of the animal								
	10—20	20—30	30—40	40—50	50—60	60—70	70—80	80—90	more than 90
0	116 C 0	119 C 0	117 C 0 118 C 0						
0.1	127 0—1	124 0—1		126 0—1	125 0—1				
0.2				132 C 2				133 C 2	
0.3				140 C 2	141 C 1—2		139 C 3 142 C 2—3		
0.5		150 C 2	147 C 2		148 C 2				149 C 2
0.7		157 C 2		158 C 2—3					156 C 2—3
0.8	163 C 1—2			164 C 3				165 C 3 166 C 3	
1.2		172 C 3—4		174 C 4				173 C 4	
1.7			180 C 4						181 C 4 182 C 4
free						111 C 4			104 C 4; 108 C 4 105 C 4; 109 C 4 106 C 4; 110 C 4

signs of atrophy visible in the connective tissue formed before the onset of scurvy.

This gradual deterioration of the collagen connective tissue manifests itself both in shape and colour. The collagen fibrils grow shorter, less regular, are often in a certain portion near the nucleus seen to be thicker than normally, or else as if they had lost their elongated form and had rolled up there. The colour is changed from the normal sparkling red, becomes a lighter pink, without gloss, and finally yellow.

It will be seen that in several cases I have hesitated to which degree to assign the strength of the connective tissue reaction. It is not always possible to decide whether the connective-tissue formation met with is pre-formed or newly-formed. The transitions between the stages fixed by me are not distinct. Often the reaction at the primary focus has been found to correspond to a certain degree, while lymph-glands afflicted later have shown a lower degree. The difference between the tendency to connective-tissue formation in different organs is also everywhere manifest, and thus the comparison must not be made directly between different organs but with the pictures given at normal connective tissue reaction of the organ in question. The figures for the strength of the reaction are therefore to a certain extent approximate. Without being stretched too far they confirm in any case in a striking manner what might already be surmised at the *post-mortem* examination, that *the strength of the connective-tissue reaction after a certain time is in a direct ratio to the dose of antiscorbutic given*. It will also seem as if for a certain case the strength of the connective-tissue reaction after a certain minimum time, about one month, were generally dependent, not so much on the lifetime after the injection, as rather on the size of the antiscorbutic dose. Here the connective tissue affords a parallel to what was proved above for the dentin. Finally it is evident, that a connective-tissue reaction of normal strength does not set in even in the latent stage (10 animals), not even with a dose of 0.8 m. pr. d. after three months. Only when the

dose of antiscorbutic given corresponds to a completely protective dose, there is a connective-tissue reaction, the strength of which is comparable to that appearing in animals on the complete control dietary (13 animals).

This connective-tissue reaction is comparatively easy to fix, thanks to the specific staining methods. About the organic changes in animals with scurvy and tuberculosis I can be brief. They are extraordinarily diversified. In the spleen, for instance, often a hundred times heavier than normally, hemorrhage, hemosiderosis, atrophy of the lymphoid tissue, hyperplasia of the reticulum, necroses, calcification, and specific granulation tissue, are all intermingled into pictures that have no resemblance to normal spleen tissue. I lack the qualifications for treating these changes in detail, nor is it in this connection necessary so to do.

Influence of tuberculosis on scurvy.

The constant presence of hemorrhages round the tuberculous foci is mentioned above (p. 112).

Besides hemorrhages, also necroses are seen near tuberculous foci, and especially small calcified necroses of muscle fibres are common in the thigh musculature of animals with scurvy and tuberculosis. Here there is, however, a change which may be seen as well with simple scurvy, though in that case not localized exactly here, as also with tuberculosis in otherwise healthy animals. It may seem probable that both diseases co-operate. Such a combination might also be supposed with regard to the appearance of necroses in the musculature in general and in the adrenals (see p. 74, 104), but we have no conclusive proof of this.

It is fairly common with extensive tuberculosis in scorbutic guinea-pigs to find granulation foci in the marrow of the ribs more or less close to the epiphyseal line. Here we often find a picture which macroscopically altogether agrees with that given by MOURIQUAND and MICHEL of the scorbutic

changes in the epiphyses. A microscopical examination at once makes it clear that this is a quite different process.

An examination of the question whether the tuberculosis, within the groups that are represented in the table 7, page 153, has aggravated the scorbutic symptoms and caused the animals to enter another stage of scurvy than that of the controls, shows that it can have been so only with regard to animals No. 148 and 149. Both these animals after 56 and 92 days have presented a scorbut extensus, whereas among the other animals with the same antiscorbutic dose two that had tuberculosis, dead after 28 and 32 days, and 3 controls, dead after 18, 92 and 92 days, respectively, only showed a scorbut levior. The fourth control animal, however, that died of septicemia after 59 days, also had scorbut extensus. Summarizing, it may be said, that the tuberculosis has shown no marked influence on the moment for the appearance of the scorbutic symptoms in different organs. When the opposite has been clinically observed (SALLE and ROSENBERG), this is probably due to a tuberculous intestinal affection with diarrhea. That in such cases antiscorbutic, given *per os*, does not show the expected effect has been stated for certain. Concerning the interpretation of this circumstance, see p. 117. For such cases the antiscorbutic may be administered otherwise than *per os* (HESS).

It may be remarked that animals 16 and 18, which had access to complete dietary but suffered from a general tuberculosis and had not increased in weight during the last month, showed slight scorbutic changes when the teeth were histologically examined. The animals were observed to eat cereal, but have probably not eaten enough of the swedes. In these cases the tuberculosis has thus indirectly caused scurvy, probably through the lessened appetite.

CHAPTER III.

Experiments on human subjects.

(Records of cases see p. 234.)

HESS says in his book: »In all nutritional investigation it should never be forgotten, that conclusions drawn from experiments on animals are merely provisional and must await substantiation on man, and furthermore, that, where differences in reaction are noted, the clinical data should be accorded full consideration.» In order further to investigate the question of the influence of scurvy on the course of tuberculosis, I have therefore carried out an experiment on human beings. In the experiment the following principle was adopted.

In a hospital for tuberculosis patients, where the diet might be suspected not to contain a completely protective dose of antiscorbutic, a number of patients (44) have been selected. I have taken them two and two together, trying to get patients as similar as possible in each couple as far as concerns age, sex, the extent and virulence of the tuberculous process, and the treatment. During the time of the year when the food in the North is most deficient in antiscorbutic, the months of March, April, and May, one of the two patients in each couple has had an orange a day added to his diet, while the other one has been given a specially prepared pastry. The clinical progress of the tuberculosis in the different cases has then been studied and compared. No immunity examinations have been made in this connection.

The experiment has been carried out in the Väsby Sanatorium in Uppland. This sanatorium has such an isolated situation that the supply of provisions from without could be controlled. For the permission to undertake the experiment at Väsby I am indebted to the Head Physician of the institutions at that place, Dr. HÅKANSSON. The physician of the Sanatorium, Dr. GUNNAR WESTBECK, has chosen the patients, made the examinations, written down the records, estimated the progress. For this and for his ungrudging and self-sacri-

ficing assistance in the whole of the experiment I owe him my best thanks.

The dietary of the Sanatorium is as follows:

At 7.30 a. m. gruel and bread
» 10 » breakfast
» 12 noon milk
» 1.30 p. m. dinner
» 4.30 » coffee with rusks or white bread
» 7 » supper.

The 70 patients of the Sanatorium (of which half the number have been selected for the experiment; the children are in a special department) consume on an average 2 litres of milk a day each. No fixed schedule of food is followed, but careful annotations are made daily of what is served, and from these annotations I have made the following extracts. Of food that might be considered to contain antiscorbutic, there has been provided during the time March 1st—May 31st 1923 (92 days):

Potatoes for *no* meal 5 days, for *one* meal 52 days, for *two* meals 35 days, in the last-mentioned case, often for one of the meals first boiled and then also fried.
Beet-root 17 times, always together with potatoes.
Beef-tea with vegetables 6 times.
Mashed roots 4 times, swedes 1 time, always together with potatoes.
Cabbage-soup 2 times, vegetable soup 2 times.
Chive 3 times.
Pears 1 time.

Among courses which for one reason or another may be considered rather unimportant as far as the supplying of antiscorbutic is concerned, may be mentioned red whortleberry jam (with Yorkshire pudding) 31 times, rhubarb mould 9 times, apple tart (dried apples) etc. 10 times, other fruit moulds 9 times, fruit-syrup sauce 3 times.

For every breakfast and supper are served vegetable margarine, hard rye-bread and cheese, rather rich, as much as is wished. Meat in some form is given once or twice daily.[1]

The dietary may be characterized as plenteous, and complete in every respect except with regard to antiscorbutic. As providing this substance there are first of all to be mentioned milk and potatoes. During this time of the year (in 1923, the cows were not turned out to grass till after the conclusion of my experiments, in June) the milk is very deficient in antiscorbutic. To arrive at a definite estimation of the quantity of antiscorbutic supplied in 2 litres of milk, is not practicable. Potatoes also are a weak antiscorbutic and do not have any

Table 10.

1	2	3	4	5	6	7
Couple	Number	Age, years	Duration of experiment, days	Stage of tuberculosis	Progress	Progress of orange case compared to control
a	1 Or.	33	89	III*	n	—
	2	32	93	III	+	
b	3 Or.	35	24	III*	n	+ ?
	4	23	60	III	—	
c	5 Or.	21	93	III	+	+
	6	20	93	III	—	
d	7 Or.	53	75	II—III*	+	+
	8	48	93	I—II	n	
e	9 Or.	44	91	III*	+	+
	10	34		I—II	n	
f	11 Or.	29	93	III	+	+
	12	28	93	III*	—	
g	13 Or.	27	91	III	+	+
	14	20	93	III	n	

[1] Meat most often given as minee-meat, first fried and then boiled.

1	2	3	4	5	6	7
Couple	Number	Age, years	Duration of experiment, days	Stage of tuberculosis	Progress	Progress of orange case compared to control
h	15 Or.	43	93	III*	+	+
	16	33	93	III	—	
i	17 Or.	25	93	III	n	+
	18	21	93	III	—	
k	19 Or.	32	93	III	+	+
	20	63	67	III	—	
l	21 Or.	20	93	II*	+	+
	22	16	93	I—II	n	
m	23 Or.	18	93	I	n	=
	24	24	93	I—II*	n	
n	25 Or.	12	77	I	n	+?
	26	16	93	I	n?	
o	27 Or.	24	93	II*	+	+
	28	28	93	I—II	n	
p	29 Or.	25	93	III*	+	+
	30	26	93	III	n	
q	31 Or.	27	93	III	+	+
	32	16	93	III	n	
r	33 Or.	7	93	III*	+	=
	34	25	93	III	+	
s	35 Or.	10	93	I	+	+
	36	11	93	I*	n	
t	37 Or.	8	92	I	+	+
	38	11	93	I	—	
u	39 Or.	4	93	I	n	=
	40	3	29	I	n	
v	41 Or.	4	93	I	+	
	42	—	—[1]	—		
w	43 Or.	12	55	I	+	+
	44	4	93	I	—	

[1] Discharged shortly after the beginning of the experiment.

considerable importance as such till consumed in rather large quantities. In any case the dietary is poor in fresh vegetables, roots and fruit.

The dietary of the children comprises an egg a day, and 3 dessert-spoonfuls of cod-liver oil.

The patients are not weighed naked, and therefore the weight figures are liable to be somewhat uncertain.

From time to time all the patients are examined with Roentgen rays; radiograms are also taken in most cases. When the Roentgen examination or the radiogram do not add essentially to the information gained by the clinical examination, they are not quoted.

The principles of the treatment have been the hygienic measures usual in Sweden. For special details, see the Records. All the children were treated with quartz lamp.

The duration of the experiment has not been extended beyond three months, as the patients do not as a rule remain in the Sanatorium above that period.

The experiments are summarized in *Table 10* (p. 166).

The figures in the first row correspond to those in the Records. All odd numbers, which furthermore are accompanied by »Or.», refer to patients who have been given an orange. The even numbers are the patients, examined for the sake of control, who instead of the orange had a pastry.

The patient who in each couple must be regarded as decidedly the graver case of the two at the beginning of the experiment is indicated by an asterisk in the fifth row, where the stage of the disease is recorded. As the patients were chosen, the graver and the lighter case was every alternate time taken as control patient within each couple.

The progress is indicated, in the sixth row, by n, + and —, according to its being corresponding to what had been expected, better or worse than was expected.

In the seventh row, the progress of the orange case as compared to that of the control patient is indicated. The sign = means that both cases have shown a corresponding progress; +, that the orange case has progressed more favour-

ably, and —, that it has progressed less favourably than the control case.

From the sixth row is seen that out of 21 control cases 11 have progressed according to expectation, while 2 have progressed better and 8 worse. It must be borne in mind that the season in question, March—May, is the time of the year which is the most trying to tuberculosis patients. The death rate for tuberculosis is then at its highest. The rather bad results among the control patients are therefore not surprising and the favourable progress in those who have had the orange is the more noteworthy. Among 22 such patients, the progress has been as expected in 6 cases, while 16 have developed more favourably than might have been expected.

In the seventh row which indicates how within each couple the disease has progressed in the orange case, in comparison with the progress of the control case, we find that the orange case had a better course in 17 instances, similar in 3, and worse in 1 instance.

Criticism. Conclusion.

Several objections might be raised against this experiment, such as its dealing with too small a number of patients and too short a time. The first objection is irrelevant, as this has been only a primary experiment which must be repeated, and I hope will be repeated in different places and with a larger material. It will then be expedient to extend the experiment over a longer period, that is to say, begin earlier in the year. The time of conclusion is fixed for experiments of this kind, viz. the beginning of the early summer. A question which carries more weight is whether the experiments have been conducted with sufficient objectiveness. In the first place it may be brought into question whether the patients have not been subjected to a suggestive influence of the orange diet, an influence which might have improved the appetite and indirectly the process. Although counter-acting measures have been adopted, this possibility can not be entirely precluded. In the second place there is the question about the objective-

ness of the investigator. I have thought the best safe-guard in this respect would be to entrust the actual examination and the judgment of the patients to an experienced specialist, and to let my own opinion carry weight in opposition to his, only when in so doing I have caused the orange cases to have a less favourable or the control cases a more favourable verdict.

Another objection is that the dietary in the sanatorium already without the orange would contain a protective dose of antiscorbutic. This objection would have been more significant if the experiment had not given a clear evidence.

Conclusion. The experiment seems to indicate that the addition of an orange to the daily fare has favourably influenced the progress of tuberculosis with a number of patients in the Väsby Sanatorium during March—May 1923. The results encourage continued investigation on a larger scale in order to gain confirmation of the theory that a sufficient amount of antiscorbutic substance in the food strengthens the resistance against tuberculosis.

Summary and conclusions of Part IV.

A tuberculosis may in different ways act on the onset or the progress of scurvy. The appetite may diminish so that a sufficient dose of antiscorbutic is not consumed. The conditions of the intestine may become changed so that the consumed dose of antiscorbutic is prevented from having an effect. A scorbutic atrophy of the vascular wall may give clinical symptoms (hemorrhages) in the neighbourhood of tuberculous foci.

In a still higher degree a scurvy appears to act upon the progress of a tuberculosis. The clinical observations, which are recorded in the literature give good grounds for supposing such an action though they have not so far been duly considered. These observations lend countenance to the notion that the resistance of the body to tuberculosis is lessened during the course of scurvy. The experiments on man which

I have undertaken point in the same direction. Experiments on a larger scale are desirable especially in regions where, like in the Northern provinces of Sweden, the fresh vegetables are as rare as the tuberculosis is frequent.

My experiments on guinea-pigs indicate that a scorbutic organism has no power of reacting against a tuberculous focus with a connective-tissue formation of normal strength. The smaller the antiscorbutic dose in the food is, the less extensive and the more inferior in quality (fibrosity) the new connective tissue becomes. This diminished faculty of healing tuberculous foci through connective tissue is apparent already early in the latent stage, a fact which is of special interest.

This deficient reaction of the connective tissue to a tuberculous irritation agrees perfectly with what has been said in the preceding part of this work with regard to the scorbutic atrophy. I am far from wishing to attribute to this deficient development of fibrous tissue alone, or even principally, the influence of scurvy on the progress of tuberculosis. It is probable that the scorbutic atrophy of other cells in the body, which are important to the resistance, also is of account. As the benignity of a tuberculous process is often measured according to its more or less pronounced fibrosity, the change in this quality through scurvy, already in the latent stage, is yet worth observing.

From a therapeutic point of view it may be said that my investigations suggest the importance of supplying a sufficient fully protective antiscorbutic dose to persons, in whom the healing of a tubercular process is aimed at. This holds true also, and perhaps particularly, with regard to early forms, for instance tuberculosis of the bronchial glands in children. Since the standard of the fully protective dose of antiscorbutic for different ages has not yet been established, it may in dubious cases be recommended rather to give a little too much than too little of suitable antiscorbutic articles of food.

PART V.

Records of cases belonging to Part I.

Extracts.

Guinea-pigs No. 1—96, Series 1—23.

Series I.

Animals 1—8. Basal diet from July 11 (No. 1—4) or August 5 (No. 5—8). Weight charts, Fig. 95.

No. 1. For this a more detailed extract from the record is given as a specimen.

♂. Black—brown—white. (The colours are mentioned in the order in which they dominate.)

$^{23}/_{7}$ The left hind-leg sometimes lifted in scurvy position. Frequent and deep breathing. Drinks but little milk. Cries out at palpation of left knee. $^{25}/_{7}$ Bad appetite. Skin dry. Coat rough. Priapism. $^{26}/_{7}$ Scurvy position of left hind-leg permanent. The upper epiphysis of left tibia fractured. Sits brooding. $^{1}/_{8}$ Getting weaker and weaker. $^{2}/_{8}$ Drags the hind quarters; falling. $^{3}/_{8}$ Mors. $^{4}/_{8}$ *Post-mortem* examination: Hair easily loosening in tufts. Body very lean. At the stripping off of the skin, *fractures* in the upper epiphyseal lines of right tibia and both humeri. Also diaphyses of the long bones more easily broken than normally. *Upper jaw* brittle (a blunt pincette easily pierces this bone as well as the bottom of the cranium). The molars of the lower jaw somewhat loose. Different joints, especially knee-joints, swollen. The swelling is localized to the adjacent epiphyses. The costochondral junctions swollen, forming a distinct rosary, most marked from the inside, partly due to an angular bend (»bayonet position«) between cartilage and bone. *Hemorrhages* numerous in subcutis and muscles. Sometimes they appear in the neighbourhood of fractures (left knee, many ribs), otherwise near the muscle connections around knees, ankles and elbows, and are numerous under pleura and pericardium viscerale. The *adipose tissue*, which is very sparse, is deeply yellow with a brownish tinge. The *heart auricles* are highly dilated. The section surface of the *liver* shows the central veins filled with blood. Otherwise nothing abnormal was remarked at the ocular examination. Microscopical examination was made of 22 ribs (Fig. 44), elbows, wrists, knees, ankles (Fig. 47), lower jaw (Fig. 34), teeth (Fig. 14, 34) muscles and liver. The staining has been hematoxylin, for the different lobes of the liver also sudan, for the ribs also methylene-blue. The description of sections from different organs forms the basis of the exposition in Part I and will not be printed here.

Diagnosis: Scorbut gravior manifestus

No. 2.

♀. Black—white—brown.

Clinical progress and macroscopical findings very like those of No. 1. Dead and autopsied $^{5}/_{8}$. Not examined microscopically.

Diagnosis: Scorbut gravior manifestus.

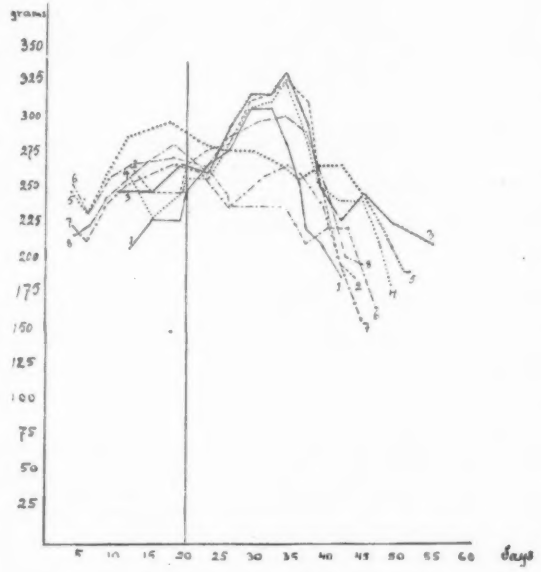


Fig. 95. Series I. No antiscorbutic.

No. 3.

♂. Brown—white—black.

Clinical progress and macroscopical findings of a nature very like the preceding numbers, though of a more pronounced degree (lifetime 38 days). Teeth very loose both in upper and lower jaw, can easily be removed with the pincette. Hemorrhages in all rib interstices, around knees and elbows. *Microscopical examination* of the same organs as in No. 1. Tooth, Fig. 31. Musculature, Fig. 57.

Diagnosis: Scorbut gravior manifestus.

No. 4.

♂. White—brown—black.

Clinical progress and macroscopical findings as in No. 3. Teeth looser still, almost falling out.

Dead and autopsied $^{10}/_{8}$. Not examined microscopically.

Diagnosis: Scorbut gravior manifestus.

No. 5.

♂. Black—brown—white.

The scurvy symptoms (joint-lesions, hemorrhages) in this case seemed still after a month comparatively little developed, but the animal was exceedingly emaciated and died $^{10}/_{9}$. Autopsied the same day: no hemorrhages. Submental lymph-glands swollen. One of them suppurated, forming an abscess large as a good-sized pea. Teeth can easily be removed. The costochondral junctions enlarged, those of the upper seven pairs show distinctly the white or yellowish white line. Otherwise as No. 1. Histological examination of the same organs as No. 1, and besides of the spleen.

Diagnosis: Scorbut gravior manifestus.

No. 6.

♂. Black—light brown.

$^{25}/_{9}$ Walks with difficulty. Dead $^{4}/_{9}$, autopsied $^{5}/_{9}$. Histological examination as in No. 5. Diaphyses of slightly increased fragility, epiphyses easily broken. Hemorrhages only in a few rib interstices. The liver contains plenty of fat. No swelling of lymph-glands. The rest as No. 5.

Diagnosis: Scorbut gravior manifestus.

No. 7.

♀. Grey—white.

Dead and autopsied $^{3}/_{9}$. Histological examination as in No. 5; spleen also stained with Giemsa. The macroscopic changes are similar to those of No. 1, only in this case there are no visceral hemorrhages and the teeth can easily be removed.

Diagnosis: Scorbut gravior manifestus.

No. 8.

♂. Grey—yellow.

Dead $^{1}/_{9}$, autopsied $^{2}/_{9}$. Hemorrhages around caput humeri dx (fracture), both scapulae, both knees and in the upper six rib interstices. The epiphyses of the long bones are easily broken, the diaphyses not. All teeth very loose. The rest as No. 1. Histological examination of the same organs as in No. 5. Besides staining of ribs with Giemsa.

Diagnosis: Scorbut gravior manifestus.

Conclusion for Series I: No antiscorbutic can be perceived in the basal diet.

Series II.

Animals 9—12, and 33 (partly). Controls on complete dietary from July 22 to December 11 (No. 9—11). September 8 to December 11 (No. 12), July 22 to October 28 (No. 33). Weight charts Fig. 96.

No. 9.

♂. Black—brown—white.

Healthy till it was chloroformed $^{11}/_{12}$. Autopsied $^{14}/_{12}$. Histological examination as in No. 7. Everywhere normal conditions.

Diagnosis: No scurvy.

No. 10.

♀. Black—white.

Pregnancy stated $^{26}/_{11}$. At the *post-mortem* examination a fetus was found in one of the uterine horns, 5 cm. from vertex to coccyx. (Fig. 32, 48). Plenty of fat peripherally in the liver acini. The rest as No. 9.

Diagnosis: No scurvy.

No. 11.

♀. White—black—brown.

Looked sound the whole time. Delivered $^{8}/_{9}$ of a lively young (No. 12). Progress, examination and findings for the rest as in No. 9. Muscle, Fig. 52; liver, Fig. 71; spleen, Fig. 79, 82.

Diagnosis: No scurvy.

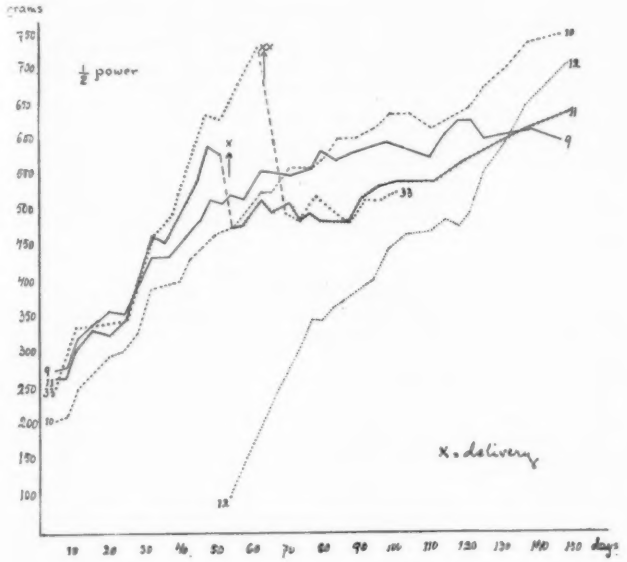


Fig. 96. Series II. >1 m. pr. d.

No. 12.

♂. Black—brown—white.

Progress, examination and findings as in No. 9 (spleen not examined histologically).

Diagnosis: No scurvy.

Conclusion for Series II: The controls have shown perfect health. No signs of scurvy, either clinically or at the patho-anatomical examination.

Series III.

Animals 13—19. Normal dietary. Were injected $^{20}/_{7}$ with tubercle bacilli, stock No. 80, received in a homogeneous emulsion from the Public Medical Institute. The absolute doses varied from 0.0000005 to 0.0025 grams of bacilli. The injection was made into the adductors of the right thigh. All the animals survived and were killed after 135 days, on $^{11}/_{12}$.

Weight charts Fig. 97. At the *post-mortem* examination no sign of another infection could be discovered, nor any sign of scurvy. Histological examination was made, besides of liver, spleen and lungs, also of a number of 11—17 ribs, knees, ankles, elbows, wrists, and lower jaw. No. 16 and 18, which had not increased in weight during the last two months, showed symptoms of scurvy at this examination. The rest showed normal bone pictures.

No. 13.

♂. Black—brown—white.

$^{29}/_{7}$ injection with 0.0000005 grams of tubercle bacilli.

Diagnosis: Tuberculosis loc. prim., lymphogland. regional., paratrachel. et submaxill., lienis. Cirrhosis hepatis initialis. No scurvy.

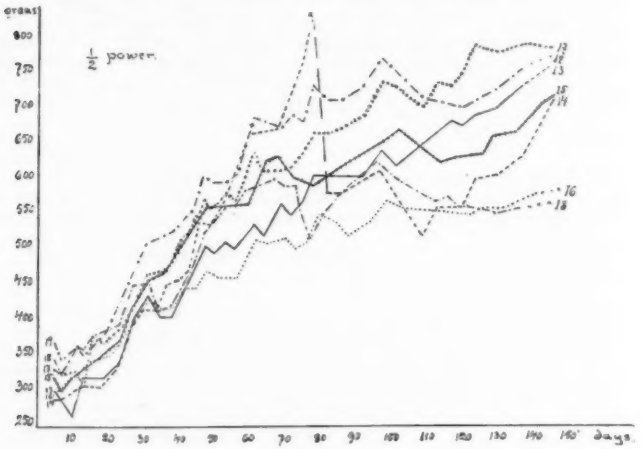


Fig. 97. Series III. > 1 m. pr. d.

No. 14.

♀. Light brown—black—white.

$^{29}/_{7}$ injection with 0.000005 grams of tubercle bacilli. $^{3}/_{9}$ Pregnant. $^{7}/_{10}$ delivered of two sturdy young ones (No. 92 and 94), that she suckled for two weeks.

Diagnosis: Tuberculosis loc. prim., lymphogland. regional., lienis. Cirrhosis hepatis initialis. No scurvy.

No. 15.

♂. Brown—black—white.

$^{29}/_{7}$ injection with 0.000025 grams of tubercle bacilli.

Diagnosis: Tuberculosis loc. prim., lymphogland. regional., lienis. Cirrhosis hepatis initialis. No scurvy.

No. 16.

♂. Light brown—white—black.

$^{29}/_{7}$ injection with 0.00005 grams of tubercle bacilli.

At the histological examination the root incisor shows a disordered odontoblast layer, the predentin is amorphously calcified amd there is a beginning formation of pulpa bone.

Diagnosis: Tuberculosis loc. prim.; lymphogland. region.; lienis, pulmonum. Cirrhosis hepatis initialis. Scorbut mitior latens levior.

No. 17.

♂. Brown—black—white.

$^{29}/_{7}$ injection with 0.00025 grams of tubercle bacilli.

Diagnosis: Tuberculosis loc. prim., lymphogland. region., lienis. Cirrhosis hepatis initialis. No scurvy.

No. 18.

♂. White—black—brown.

$^{29}/_{7}$ injection with 0.0005 grams of tubercle bacilli.

At the histological examination the same changes are seen in the incisor root as in No. 16. In the costochondral junction the cartilage columns are seen in disorder.

Diagnosis: Tuberculosis loc. prim.; lymphogland. region.; lienis, hepatis, pulmonum, testium. Scorbut mitior latens extensus.

No. 19.

♂. White—light brown.

$^{29}/_{7}$ injection with 0.0025 grams of tubercle bacilli.

At the *post-mortem* examination the incisors of the lower jaw are found to be somewhat loose. Histological examination of these shows a normal picture.

Diagnosis: Tuberculosis loc. prim., lymphogland. region., lienis, hepatis, pulmon. No scurvy.

Conclusion for Series III: The consequence of an injection of tubercle bacilli has been a tuberculosis which, when the animals were killed after 135 days, has left distinct marks in the local focus, lymphglands, spleen and liver, with higher dosage also in other organs. The liver changes with the smaller dosages consist of an interacinous increase of the connective tissue. With the higher dosages this connective tissue in some places assumes the character of tuberculous granulation tissue. The three animals which showed general tuberculosis (No. 16, 18, 19) did not increase in weight during the last month. In any case the virulence of the bacilli must be indicated as rather weak. One animal (No. 14) even went through a delivery followed by three weeks' suckling of twins, and afterwards went on well.

Series IV.

Animals 20—23. From August 8 basal diet + 1 ccm. of red whortleberry juice bought at grocer's. Weight charts, Fig. 98.

All four proceeded as cases of typical scurvy to death after 26 to 30 days and showed, at the *post-mortem* examination (teeth that were easily removed, extensive hemorrhages, swollen joints, enlarged costochondral junctions with white lines, fragile epiphyses and, to a smaller degree, diaphyses, etc.) as well as at the histological examination of the same organs as in No. 5, the typical signs of scurvy. (No. 22 not microscopically examined.)

No. 20.

♂. White—black.

Dead and autopsied $^{5}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

No. 21.

♀. White (albino).
Dead $^{2}/_{9}$, autopsied $^{8}/_{9}$. Spleen also stained with Giemsa.
Diagnosis: Scorbut manifestus gravior.

No. 22.

♂. Light brown—white.
Dead and autopsied $^{5}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

No. 23.

♀. White—light brown—black.
Dead and autopsied $^{7}/_{9}$. Tooth, Fig. 17; muscles, Fig. 54.
Diagnosis: Scorbut manifestus gravior.

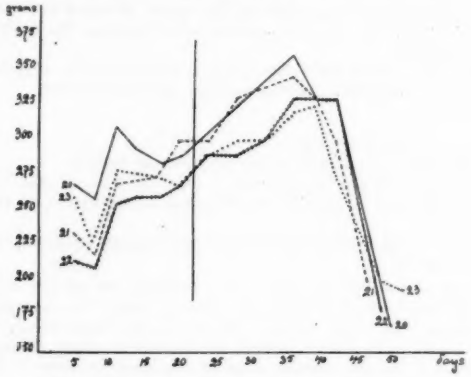


Fig. 98. Series IV. No antiscorbutic.

Conclusion for Series IV: The dosage administered (1 ccm.) of red whortleberry juice with the origin mentioned has not had any perceptible antiscorbutic effect.

Series V.

Animals 24—27. From August 8, basal diet and besides 5 ccm. each of the same red whortleberry juice as in Series 4. Weight charts, Fig. 99.

All four proceeded as typical cases of scurvy to death in 24 to 27 days. At the *post-mortem* examination they all showed extensive hemorrhages in the intercostal musculature, in the muscles round the knees, ankles, elbows and scapulae; No. 24 also extensive hemorrhages subcutaneously and under the tongue epithelium. The picture for the rest like that shown in Series IV, also at the histological examination of organs mentioned there.

No. 24.

♀. White—black—light brown.
Dead and autopsied $^{5}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

No. 25.

♂. Black—light brown.
Dead and autopsied $^{5}/_{9}$. Tooth, Fig. 9.
Diagnosis: Scorbut manifestus gravior.

No. 26.

♂. Light brown.
Dead and autopsied $^{6}/_{9}$. The marrow of the ribs also stained with Giemsa.
Diagnosis: Scorbut manifestus gravior.

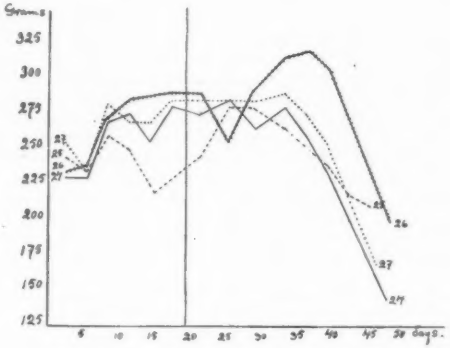


Fig. 99. Series V. No antiscorbutic.

No. 27.

♀. White—greyish brown.
Dead $^{4}/_{9}$, autopsied $^{5}/_{9}$. After $^{19}/_{8}$ the animal had a slight cough. The spleen picture confirms the surmise that an infection has been present. The marrow of the ribs also stained with Giemsa.
Diagnosis: Scorbut manifestus gravior. Infectio.

Conclusion for Series V: The dosage administered (5 ccm.) of red whortleberry juice with the origin mentioned has not had any perceptible antiscorbutic effect.

Series VI.

Animals 28—33. They got from different dates basal diet and besides 10 ccm. of the same juice that had been given in the two preceding series. Weight charts, Fig. 100.

No. 28.

♀. Black—white.
The animal was put $^{11}/_{7}$ on solely basal diet and with this diet developed scurvy symptoms. $^{17}/_{7}$ keeping still. $^{23}/_{7}$ tenderness of right knee. $^{24}/_{7}$ lame; does not finish its milk. $^{29}/_{7}$ very dishevelled; swallows its faeces; pronounced oliguria. $^{30}/_{7}$ 10 ccm. of the above-mentioned juice was

given. $^{30}/_{7}$ scurvy position of left hind-leg. $^{1}/_{8}$ less dishevelled, somewhat livelier movements. $^{6}/_{8}$ oliguria lessened. $^{13}/_{8}$ mors. Autopsied $^{14}/_{8}$, the examination showed very marked scorbutic changes, like those in Series IV and V, likewise the histological examination of all ribs, knees, ankles, elbows, wrists, jaw and liver. Musculature, Fig. 53. Nowhere an effect of the antiscorbutic can be traced. The clinically observable changes which set in with the administering of the juice — the animal became livelier, passed a larger quantity of urine and had a less dishevelled coat — is not necessarily owing to an antiscorbutic effect. The animal died 32 days after the first alteration of the diet, a fortnight after it had the whortleberry juice.

Diagnosis: Scorbut manifestus gravior.

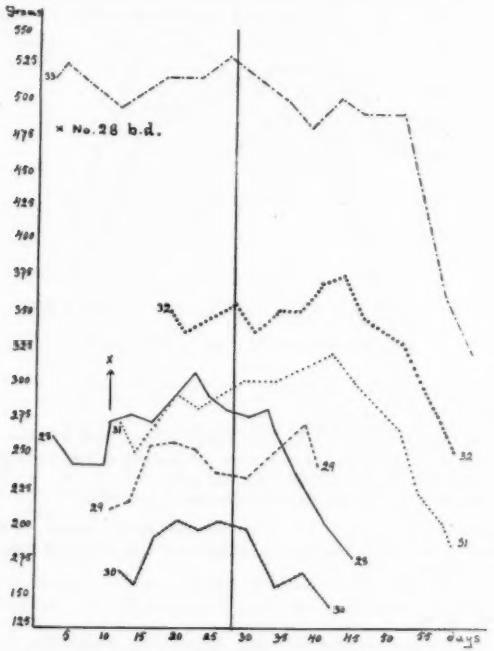


Fig. 100. Series VI. No antiscorbutic.

No. 29.

♀. Light brown—white.

$^{8}/_{8}$ put on basal diet with an addition of 10 ccm. of red whortleberry juice. On that date the animal had decreased in weight for a week back (infection). It died after 12 days, $^{20}/_{8}$, and was autopsied the same day. Teeth firm, no signs of scurvy. The animal was fairly fat and generally showed normal conditions. The right lung adhered to the chest wall through

a fibropurulent exudate. In the left pleura a sparse hemorrhagic exudate. On the pericardium a film of fibrin. In both lungs numerous small pneumoniae, partly forming abscesses. Spleen somewhat enlarged. At the histological examination of the epiphyseal ends of the long bones, the bone columns are found to be somewhat thin, the bone marrow rather bright. Root of a tooth, Fig. 5. Hemorrhages in the rib musculature, otherwise none. Hyperplasia of the spleen. Liver: diffuse fat, all over staining badly.

Diagnosis: Scorbut latens gravior, bronchopneumoniæ bilaterales c. pleurit., pericarditis.

No. 30.

♀. White—light brown—black.

Put on basal diet $^{8}/_{8}$, with an addition of 10 ccm. red whortleberry juice. On that date the animal had remained at the same weight a week. $^{21}/_{8}$ conjunctivitis purulenta. $^{22}/_{8}$ dead, a fortnight after beginning with the diet. *Post-mortem* examination the same day. No adipose tissue except around the kidneys. Purulent exudate in the conjunctiva. Pea-sized abscesses in the submaxillary lymph-glands. Hyperemia in the lungs, diminished air content. Irregular sore in the mucous membrane of the cæcum in its most oral part with necrotic bottom, passing over to the adjacent part of the small intestine. The corresponding part of the serosa has a purulent film; hyperemia in the mesentery. Possibly some swelling of the upper epiphyseal line of the tibia. The epiphyseal ends of the long bones are more easily broken than normally. The upper back molar on the right rather loose.

Diagnosis: Scorbut latens gravior; septicemia.

No. 31.

♂. Black—white.

$^{8}/_{8}$ put on basal diet with an addition of 10 ccm. of whortleberry juice. Typical progress of scurvy. $^{1}/_{9}$ diarrhea. $^{7}/_{9}$ died and was autopsied. Macro- and microscopical examination as in Series V. Liver enormously fatty.

Diagnosis: Scorbut manifestus gravior; infectio.

No. 32.

♂. White—black—brown.

$^{25}/_{8}$ put on basal diet with an addition of 10 ccm. of whortleberry juice. Showing the picture of uncomplicated scurvy it proceeded to death after 31 days, $^{25}/_{9}$, and was autopsied the same day. The *post-mortem* examination could not be concluded.

Diagnosis: Scorbut manifestus gravior.

No. 33.

♀. At first fed during 160 days on complete diet (weight chart, Fig. 96). During this time she was delivered of twins (No. 91 and 93), and showed every sign of health. Put on basal diet $^{28}/_{10}$ with 10 ccm. of the whortleberry juice. Had scurvy symptoms and died after 32 days, $^{3}/_{12}$. Autopsied the same day, showing the same picture as the animals in Series V. No histological examination.

Diagnosis: Scorbut manifestus gravior.

Conclusion for Series VI: The dosage administered (10 ccm.) of red whortleberry juice with the origin mentioned has had no perceptible antiscorbutic effect.

Series VII.

Animals 34—37. The animals had from August 31 5 ccm. raw fresh juice, immediately before the feeding pressed from red whortleberries bought in the market-place. Progress, findings at *post-mortem* examination, histological picture similar to those in Series V. Weight charts, Fig. 101.

No. 34.

♀. Yellow—black—white.
Died $^{7}/_{10}$, autopsied $^{8}/_{10}$.
Diagnosis: Scorbut manifestus gravior.

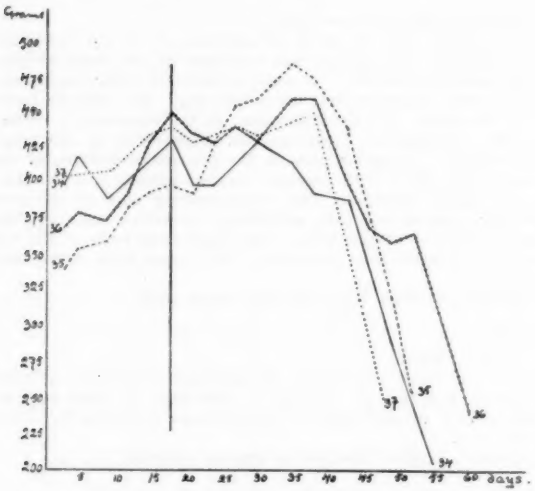


Fig. 101. Series VII. No antiscorbutic.

No. 35.

♂. Yellow—black—white.
Died and was autopsied $^{5}/_{10}$. Musculature, Fig. 62; liver, Fig. 73.
Diagnosis: Scorbut manifestus gravior.

No. 36.

♂. Yellow—black—white.
Died and was autopsied $^{13}/_{20}$.
Diagnosis: Scorbut manifestus gravior.

No. 37.

Brown—white—black.
Died $^{30}/_{9}$. Autopsied $^{1}/_{10}$.
Diagnosis: Scorbut manifestus gravior.

Conclusion for Series VII: The animals have lived on an average 37 days, which is rather a long lifetime for animals on scurvy diet. It ought

to be observed that the animals in this series were heavier than the rest. No marked antiscorbutic effect of the fresh, raw juice of red whortleberries could be perceived.

Series VIII.

Animals 38—41. The animals got basal diet from August 8, and besides each 2 ccm. of the juice from red whortleberries which had been bottled nearly a year in water. The juice was pressed out of the berries immediately before the feeding. Histological examination of the same organs as in Series V. Weight charts, Fig. 102.

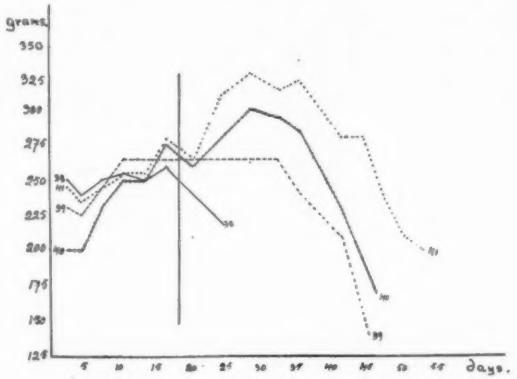


Fig. 102. Series VIII. No antiscorbutic.

No. 38.

♀. Black—light brown.

Kept in the same cage as No. 64, which died $^{13}/_{8}$ of acute infection. Died and was autopsied $^{16}/_{8}$. No sign of scurvy was seen macroscopically. In the small intestine highly injected vessels and ulcerations of the mucous membrane, corresponding to the localization of faecal lumps. Histological examination: root of a tooth, Fig. 4. The liver shows to a large extent the picture of acute necrosis.

Diagnosis: Scorbut latens gravior.

No. 39.

♂. Black—white—brown.

Progress, examination and findings similar to those in Series V. Died $^{4}/_{9}$, autopsied $^{5}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

No. 40.

♂. Brown—black—white.

Progress, examination and findings similar to those of Series V. Died $^{5}/_{9}$, autopsied $^{6}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

No. 41.

♀. Black—brown—white.

Progress, examination and findings similar to those of Series V. Died $^{14}/_{9}$, autopsied $^{15}/_{9}$. Liver, Fig. 72, also stained for iron. Spleen, Fig. 81, 83; stained according to Giemsa and on amyloid.

Diagnosis: Scorbut manifestus gravior.

Conclusion for Series VIII: No antiscorbutic effect was observed from 2 ccm. of the juice pressed in 1922 from berries preserved in water since 1921.

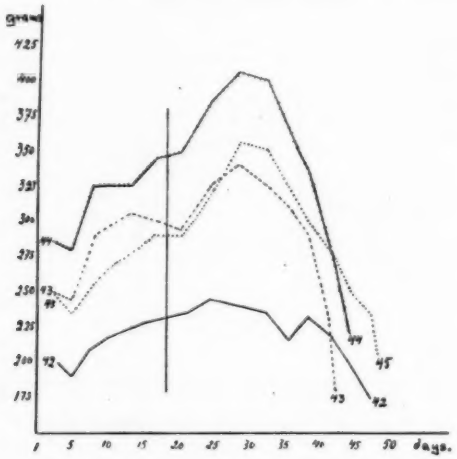


Fig. 103. Series IX. No antiscorbutic.

Series IX.

Animals 42—45. The animals had basal diet from August 8, with an addition of 7 ccm. of the same juice as Series VIII. Weight charts, Fig. 103. Progress, examination and findings similar to those in Series V.

No. 42.

♂. White—black—yellow.
Dead and autopsied $^{6}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

No. 43.

♂. Yellow—white—grey.
Dead and autopsied $^{2}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

No. 44.

♂. Grey—white—brown.
Dead and autopsied $^{8}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

No. 45.

♂. Black—white—brown.

Dead and autopsied $^{7}/_{9}$. Liver, Fig. 74. Adrenal examined on iron.

Diagnosis: Scorbut manifestus gravior.

Conclusion for Series IX: In a dosage of 7 ccm., the whortleberry juice tested in Series VIII did not produce an antiscorbutic effect any more than in that series.

Series X.

Animals 46—49. Had basal diet from August 8, and besides 5 ccm. of a juice which at the beginning of the experiment was pressed from berries stirred raw, in the autumn of 1921, with the same quantity of sugar for an hour, and afterwards kept in a glazed jar, tied over with waxed paper. Weight charts, Fig. 104. These charts all show the form which appears when an animal with an acute infection is put on scurvy diet. The initial rising of the weight curve is missing.

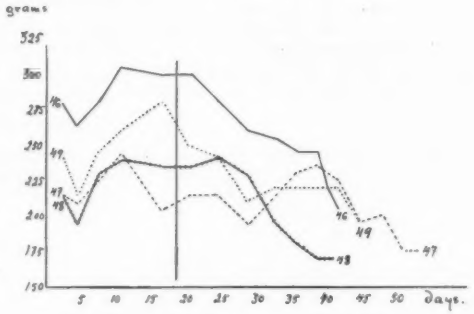


Fig. 104. Series X. No antiscorbutic.

No. 46.

♂. Black—white—brown.

$^{25}/_{8}$ walks with difficulty; dishevelled. $^{29}/_{8}$ groaning, laborious breathing. Restless. $^{31}/_{8}$ dead. $^{1}/_{9}$ autopsied. Not very lean. A submaxillary lymph-gland forms an abscess. Right lung pneumonic, in the left lung an abscess, with a diameter of 5 mm. Three ulcerations in the large intestine. The epiphyses of the long bones easily breaking, the diaphyses not. The upper jaw brittle. Teeth loose; the upper molars are easily lifted out. Pyorrhea around the dental sac of the upper, loosened incisors. No hemorrhages. Knee joints somewhat swollen.

Diagnosis: Scorbut manifestus gravior. Septicemia.

No. 47.

♀. White—black—brown.

Progress and findings typically scorbutic, similar to Series V. No histological examination.

Diagnosis: Scorbut manifestus gravior.

No. 48.

♀. White—black—yellow.

After a week less lively, grew gradually weaker and after 22 days was found one morning lying flattened underneath its fellows. *The post-mortem* examination on the same day showed multiple hemorrhages in the upper three rib interstices on the left side and around the left scapula. Fracture of one tibia in the upper epiphysis. Other epiphyses of the long bones easily broken, upper jaw brittle. Some of the teeth loose. Venous stasis in the thorax. Histological examination as in Series V. Musculature, Fig. 59.

Diagnosis: Scorbut manifestus gravior. Infectio? Suffocatio.

No. 49.

♀. White—black.

Progress as in the preceding case. Dead $^{5}/_{9}$, autopsied the same day. Emaciated. Purulent submaxillary lymphadenitis. Fracture of one wrist when taken out. For the rest only slightly increased fragility of the epiphyses of the long bones. Teeth loose. No hemorrhages. Hyperemia around the 5 upper anterior costochondral junctions on both sides. Lively hyperemia of the colon and its mesentery. The mucous membrane in this place swollen and reddened. Histological examination as in Series V.

Diagnosis: Scorbut manifestus gravior. Lymphadenitis suppur. Colitis.

Conclusion for Series X. No antiscorbutic effect observed from 5 ccm. of juice from red whortleberries a year old, stirred with sugar.

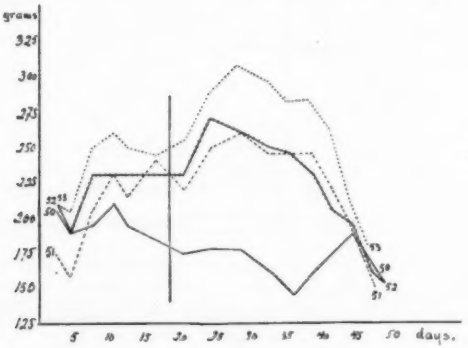


Fig. 105. Serier XI. No antiscorbutic.

Series XI.

Animals 50—53. Got basal diet from August 8, and besides the juice of fresh raw blue whortleberries, bought every two or three days in the market-place. Weight charts, Fig. 105. Progress, examination and findings similar to those in Series V.

No. 50.

♀. Brown—black—white.

Died and was autopsied $^{7}/_{9}$. In the seventh and eighth rib interstices

on the right side grains in the musculature of a granulary, whitish yellow mass (calcium), in shape and size like a threepenny bit. Around this there were hemorrhages into the musculature. Tooth, Fig. 15, 16.

Diagnosis: Scorbut manifestus gravior.

No. 51.

♀. Brown—white—black.
Dead and autopsied $^{6}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

No. 52.

♀. All white (albino).
Suffered from diarrhea during a couple of days from $^{1}/_{9}$. Died $^{6}/_{9}$, autopsied $^{7}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

No. 53.

♂. Greyish brown.
Died $^{5}/_{9}$, was autopsied $^{6}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

Conclusion for Series XI: No antiscorbutic effect has been observed from fresh blue whortleberry juice of the year 1922, in a dosage of 1 ccm.

Series XII.

Animals 54—57. Had basal diet from August 8, together with 5 ccm. of the juice from fresh blue whortleberries bought in the market. Weight charts, Fig. 106.

No. 54.

♀. White—black—brown.
Showed continuous emaciation and increasing difficulty of moving, till it was found $^{27}/_{8}$ flattened out beneath its fellows. The *post-mortem* examination the next day showed no hemorrhages. Swelling of the two uppermost pairs of the costochondral junctions and of the epiphyseal ends at the knees. The back molars in the lower jaw slightly loosened. Two lymph-glands in the mesentery of the large intestine somewhat swollen, lentil-sized. Venous stasis in the thorax. Histological examination of the same organs as in Series V.

Diagnosis: Scorbut manifestus gravior. Infectio.

No. 55.

♀. White—brown—black.
Progressed to death in 35 days with typical scurvy symptoms. Dead $^{12}/_{9}$, autopsied $^{13}/_{9}$. Findings and histological examination similar to those in Series V.

Diagnosis: Scorbut manifestus gravior. Infectio.

No. 56.

♀. Brown—black—white.
Dead $^{9}/_{9}$, autopsied $^{12}/_{9}$. Progress, findings at *post-mortem* and histological examination similar to those in Series V.

Diagnosis: Scorbut manifestus gravior.

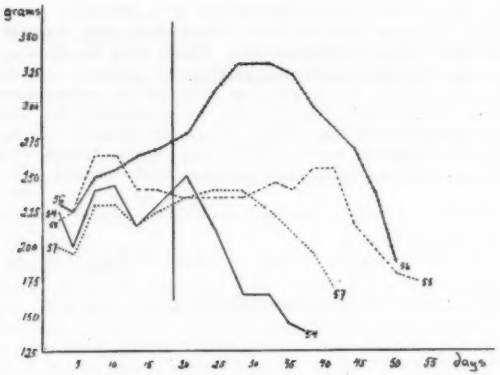


Fig. 106. Series XII. No antiscorbutic.

No. 57.

♀. Brown—black—white.

31/8 a rhinitis was observed. Dead the same day. Progress like that of Series V. At the *post-mortem* examination hundreds of small and large hemorrhages were seen in the periosteum, perinephrically, around the considerably enlarged costochondral junctions and the epiphyseal ends of the long bones which were very brittle, etc. Histological examination as in Series V. Tooth, Fig. 12 and 13.

Diagnosis: Scorbut manifestus gravior. Rhinitis ac.

Conclusion for Series XII: No antiscorbutic effect could be stated of 5 ccm. of juice from fresh blue whortleberries of the year 1922.

Series XIII.

Animals 58—61. From August 8, they got juice from blue whortleberries, stewed for one hour in 1921 and then kept for a year in a glazed jar, tied over with waxed paper. Weight charts, Fig. 107. The animals reached the maximum weight after 23—26 days; displayed scurvy symptoms, though later than the animals in the preceding series, and died after 60, 52, 39, and 61 days, respectively.

No. 58.

♀. White—brown—black.

Dead 7/10, autopsied 9/10. Highly marked scurvy changes, teeth very loose, the epiphyses of the long bones very swollen and brittle, etc. At the costæ II, IV, VI, VIII sin., VI dx, about 1 cm. from the costochondral junction, lentil-sized grains of a dry whitish yellow mass (calcium) lying against the bared bone. Closer to the costochondral junction the intercostal musculature is locally swelled in several interstices, and pale. Histological examination as in Series V. Tooth, Fig. 8; muscle, Fig. 56, 58; spleen, Fig. 81. Spleen also stained on iron, amyloid, and according to Giemsa. Staining on iron also of knees and ribs.

Diagnosis: Scorbut manifestus mitior.

No. 59.

♂. White—yellow—black.

In dying condition killed with ether $^{29}/_{9}$. Autopsied immediately. Progress and findings very like No. 58. Around the enlarged costochondral junctions in the fifth to eighth interstices on the right side, the intercostal musculature was found to be swelled into exorbitant, pale greyish-pink masses, which to the width of about 1 mm. filled the space between the ribs. Histological examination as in No. 58.

Diagnosis: Scorbut manifestus mitior.

No. 60.

♀. White—yellow—black.

Progress, findings and histological examination similar to the two preceding numbers. Died $^{16}/_{9}$, autopsied $^{17}/_{9}$. Lymphoglandula submentalis forms a pea-sized abscess. Around the sixth and seventh ribs on the right, fourth to eighth on the left side, enlargements similar to those described above lying in the intercostal musculature below the fascia, here they look like processes from the boundary line.

Diagnosis: Scorbut manifestus mitior. Lymphadenit. ac. purulenta submental.

No. 61.

♂. Grey—brown.

Dead $^{4}/_{10}$, autopsied $^{5}/_{10}$. Progress and findings similar to No. 58. Around the seven upper ribs on both sides, near the costochondral junctions, enlargements in the intercostal musculature looking like young connective tissue. No histological examination undertaken.

Diagnosis: Scorbut manifestus mitior.

Conclusion for Series XIII: The juice of blue whortleberry compote, a year old, in a dosage of 5 ccm. has proved to be of a certain antiscorbutic value (0.1 m. pr. d.).

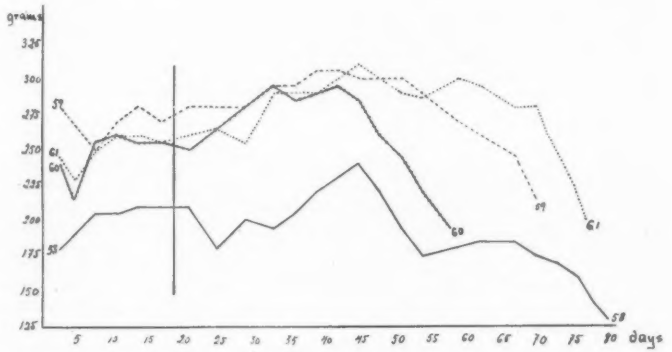


Fig. 107. Series XIII. 0.1 m. pr. d.

Series XIV.

Animals 62—66. Got basal diet together with 10 ccm. of the same blue whortleberry juice as the animals in Series XIII; No. 62—65 from August 8, No. 66 from August 25. Weight charts, Fig. 108.

No. 62.

♂. **Black—brown—white.**

Got lean without showing signs of scurvy. Was found dead $^{19}/_{8}$, flattened out beneath its fellows, and was autopsied the same day. At the *post-mortem* examination there was no sign of scurvy or infection. Histological examination of teeth.

Diagnosis: **Scorbut mitior latens levior. Infectio?**

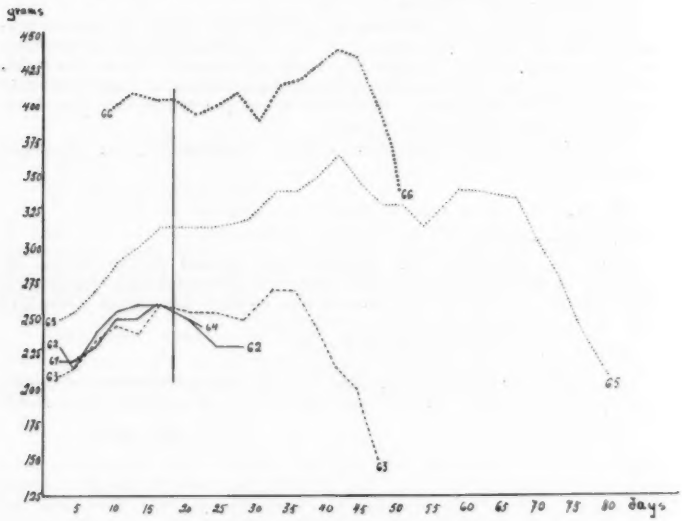


Fig. 108. Series XIV. 0.2 m. pr. d.

No. 63.

♀. **Grey.**

$^{25}/_{8}$ not very lively, dishevelled and dry. $^{26}/_{8}$ lymphogland. submental. as big as a good-sized pea, $^{27}/_{8}$ as a bean. Operated $^{27}/_{8}$ (ethyl chlorid): an attempt to extirpate the purulent gland entire did not succeed. Tamponade. $^{28}/_{8}$ improved; eats; walks about. $^{31}/_{8}$ lively. $^{3}/_{9}$ joints not swollen or tender. $^{6}/_{9}$ dead and autopsied. From the operation aperture upwards to the bottom of the mouth an abscess cavity, the size of an almond. Macroscopically the back molars in the lower jaw were found rather loose. Histological examination as in Series V shows marked scorbutic pictures. Musculature, Fig. 60.

Diagnosis: **Scorbut mitior latens extensus. Lymphadenitis submental. suppur.**

No. 64.

♀. Brown—white.

Died already $^{12}/_{8}$, flattened against the floor. *Post-mortem* examination the same day showed a row of purulent lymph-glands on both sides of the neck. The mucous membrane in the larynx reddened. Histological examination of the same organs as in Series V, and besides of lungs.

Diagnosis: Scorbut initialis. Lymphadenit. supp. colli.

No. 65.

♀. Grey.

$^{25}/_{8}$ not very lively, coat dishevelled. $^{2}/_{9}$ the upper epiphyses of tibiæ swollen, tender. Walks slowly and awkwardly. $^{5}/_{10}$ dead and autopsied: no sign of infection. Very strongly marked scurvy changes, hemorrhages around all ribs, knees and ankles; loose teeth, brittle bones, swollen joints and costochondral junctions etc. Histological examination as in Series V.

Diagnosis: Scorbut manifestus mitior.

No. 66.

♀. Brown—white—black.

Showed hardly distinct scurvy symptoms (a slight swelling of the knees) before death $^{26}/_{9}$. The *post-mortem* examination the same day showed small hemorrhages on the patellæ and in a couple of rib interstices, slightly swollen knees, rather strong enlargement of the costochondral junctions with the white line; teeth firm. Besides, sign of infection of the upper respiratory canal and bronchopneumonia. Histological examination as in Series V and also of lungs and different lymph-glands.

Diagnosis: Scorbut manifestus mitior. Bronchopneumoniae ac.

Conclusion for Series XIV: The slight degree of scurvy shown by No. 63, is remarkable. The juice of stewed blue whortleberries from 1921 has in this case, as well as in No. 66, had a certain antiscorbutic effect.

Series XV.

Animals 67—70. From August 8 basal diet together with a daily dose each of 5 ccm. of wood-strawberry juice. The first three weeks this juice was pressed from fresh strawberries, afterwards from berries that had been stirred early in August for one hour together with the same quantity of sugar, and had been kept in a glazed jar tied over with waxed paper. Already before three weeks had gone, the animals had become less lively. Soon after they developed distinct scurvy symptoms. Weight charts, Fig. 109.

No. 67.

♀. White—brown—black.

Dead $^{10}/_{9}$, autopsied $^{20}/_{9}$. Findings and histological examination similar to those in Series V. Ecchymoses in the mucous membrane of the ventricle. At the ribs II sin. and IV—VI bilat., around the costochondral junctions there are seen rounded or cuneiform swellings of the intercostal musculature. Jaw, Fig. 33.

Diagnosis: Scorbut manifestus mitior.

No. 68.

♀. White—black—brown.

Dead and autopsied $^{28}/_{9}$. Progress, findings and histological examination as in No. 67. The change described around the costochondral junctions

is only seen around rib VI dx. No hemorrhages in internal organs. Spleen also stained according to Giemsa. Radiograms of the ribs, Fig. 42, a.

Diagnosis: Scorbut manifestus mitior.

No. 69.

♀. Yellow—grey.

Dead and autopsied $^{27}/_{9}$. Progress, findings and histological examination very similar to No. 63. Ribs, Fig. 41.

Diagnosis: Scorbut manifestus mitior.

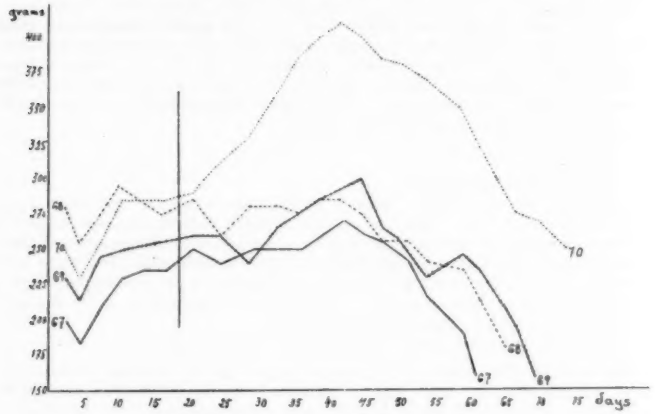


Fig. 109. Series XV. 0.1 m. pr. d.

No. 70.

♀. Black—white—brown.

$^{25}/_{8}$ less lively. $^{12}/_{9}$ knees swollen. $^{20}/_{9}$ knees very swollen and tender. Dead and autopsied $^{2}/_{10}$. Hemorrhages around nearly all ribs, knees, elbows, subpleurally on both lungs; knees so brittle that they break into small pieces when taken out. No swelling of the intercostal musculature. Teeth easily lifted out, etc. Histological examination as in Series V.

Diagnosis: Scorbut manifestus mitior.

Conclusion for Series XV: The juice of wood-strawberries from the year 1922 has shown a certain antiscorbutic effect.

Series XVI.

Animals 71—74. From August 25, basal diet and besides a daily dose each of 5 ccm. of fir needle decoction (see p. 24). Weight charts, Fig. 110. Progress, findings and histological examination similar to Series V, yet a smaller number of bones have been examined.

No. 71.

♂. Black—brown—white.

Dead and autopsied $^{23}/_{9}$.

Diagnosis: Scorbut manifestus gravior.

No. 72.

♀. Brown—grey—white.
Dead $^{26}/_{9}$, autopsied $^{27}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

No. 73.

♂. White—black—brown.
Dead and autopsied $^{25}/_{9}$. Liver, Fig. 77. Also staining on iron of liver and spleen; spleen likewise on amyloid and, as also the marrow of the ribs, according to Giemsa.
Diagnosis: Scorbut manifestus gravior.

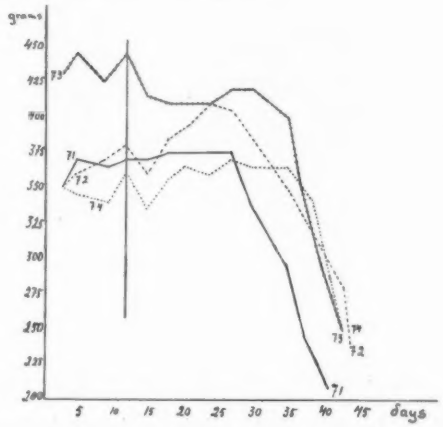


Fig. 110. Series XVI. No antiscorbutic.

No. 74.

♂. Brown—white—black.
Dead $^{24}/_{9}$, autopsied $^{25}/_{9}$.
Diagnosis: Scorbut manifestus gravior.

Conclusion for Series XVI: The fir needle decoction in a dosage of 5 ccm. has shown no antiscorbutic effect.

Series XVII.

Animals 75—78. They got, from October 4 to October 29, a daily dose each of 1 ccm. of fresh juice from somewhat dry oranges; October 29 to November 18, 8 ccm. of preserved orange juice, after November 18 again fresh juice, now from juicy oranges (see p. 26). Weight charts, Fig. 111. After October 29, the weight of all the animals went down within a week. On November 18, they all showed pronounced signs of scurvy, which were more strongly marked in No. 75 than in the rest. This animal died $^{19}/_{11}$, whereas the others after a few days again seemed lively.

No. 75.

♂. Yellow—white—black.

Dead and autopsied $^{10}/_{11}$. Hemorrhages around a number of ribs. The costochondral junctions enlarged, except those of the lowest pairs. Pale connective-tissue formations around several ribs, most pronounced around VI dx. Teeth loose, except the anterior upper molars. Histological examination as in Series V. Teeth and ribs also stained according to Hansen, the ribs besides with Weigert's fibrin stain and on iron. Tooth, Fig. 18; ribs, Fig. 45, Plate II.

Diagnosis: Scorbut manifestus mitior.

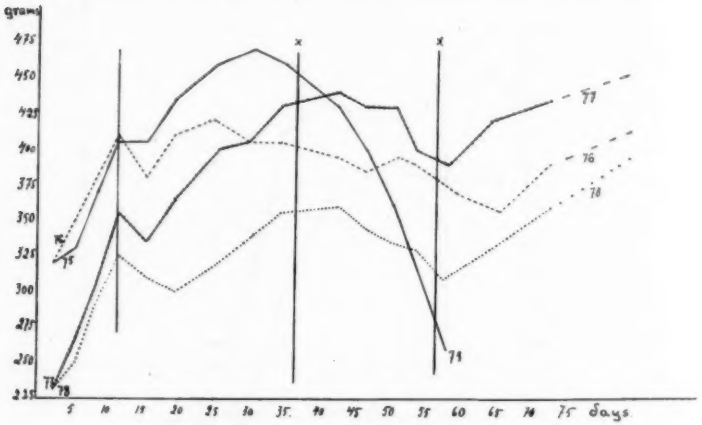


Fig. 111. Series XVII. Varied antiscorbutic dose.

No. 76.

♂. White—light brown—grey.

Chloroformed $^{11}/_{11}$ and autopsied the same day. Macroscopically no sign of scurvy. Histological examination as in No. 75. Tooth, Fig. 19, 20; ribs Fig. 46 a, Plate I.

Diagnosis: Healing scurvy.

No. 77.

♂. White—black—yellow.

Progress, findings and examination as in No. 76. Incisors rather brittle. Ribs, Fig. 46 b; musculature, Fig. 63, 64.

Diagnosis: Healing scurvy.

No. 78.

♂. White (albino).

Progress, findings and examination as in No. 76, but incisors somewhat loose. Tooth, Fig. 21.

Diagnosis: Healing scurvy.

Conclusion for Series XVII: No more than other products of the vegetable kingdom, oranges can be said to exercise a constant antiscorbutic effect. The antiscorbutic value evidently may vary.

Series XVIII.

Animals 76—82, They got a modified basal diet from October 12, the cod-liver oil being excluded. With this basal diet the animals had fresh orange juice, No. 79 and 80 2 ccm., No. 81 and 82 4 ccm. From October 29 to November 18, they had instead of the fresh juice 8 ccm. of preserved juice as in Series XVII. The two first animals died during this time, 30 and 19 days, respectively, after the starting of the experiment, of acute infections. After November 18, the two others again had fresh juice, in a dose of 4 ccm. Weight charts, Fig. 112.

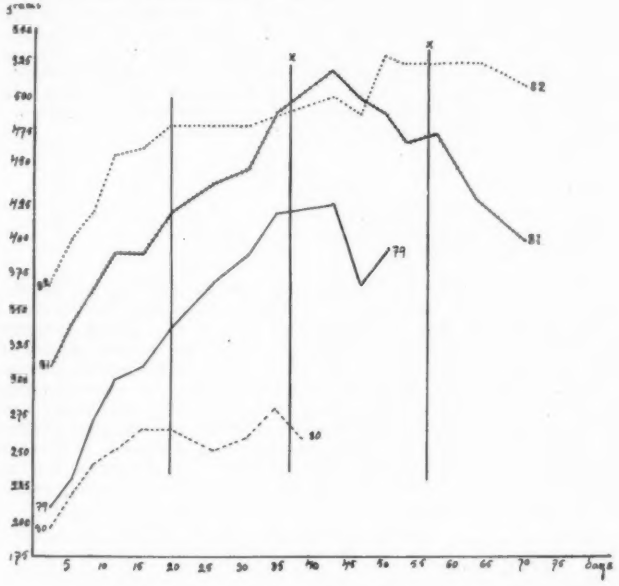


Fig. 112. Series XVIII. Varied antiscorbutic dose.

No. 79.

♀. Black—white—brown.

Dead $^{11}/_{11}$, autopsied $^{12}/_{11}$. Abdomen considerably swollen. Intestine highly distended by gas. In the abdominal cavity some ccm. of turbid fluid. Peritoneum viscerale et parietale rose-coloured. Neither clinically nor at the *post-mortem* examination any scorbutic symptoms are seen, no more at the histological examination, undertaken as in Series V, except in the teeth.

Diagnosis: Scorbut mitior latens levior. Peritonitis diffusa.

No. 80.

♂. White—yellow—black.

Dead $^{1}/_{11}$, autopsied $^{5}/_{11}$. Altogether parallel with No. 79, the only

difference being that No. 80 has normal abdomen, a pneumonic right lung and cellular infiltration in the tongue musculature.

Diagnosis: Scorbut latens levior; glossitis; pneumonia ac.

No. 81.

♂. Grey—yellow—white.

Towards the end of the period when preserved juice was given, the animal decreased in weight and in liveliness. Grew livelier after the supply of fresh juice. but continued losing in weight. Chloroformed $^{11}/_{12}$; autopsied $^{14}/_{12}$. Very lean but otherwise normal. No sign of infection, nor of scurvy. At the histological examination as in Series V, nothing was seen that recalled scurvy, except in the ribs. The odontoblast layer of the teeth completely in order. The dentin showed unequally bright strata, with uneven edge inwards; Tomes' canals somewhat widened. The epiphyses of the long bones without remark, except those of the ribs. Here the cartilage columns are short, the bone deposit sparse, in some places a bone plate is seen stretching transversely along the end of the cartilage.

Diagnosis: No scurvy.

No. 82.

♂. Yellow—white—black.

The same progress and findings as in No. 81.

Diagnosis: No scurvy.

Conclusion for Series XVIII: The animals have for 30, 19, 60 and 60 days suffered from the want of A-vitamin. The first two animals that had an unsufficient dose of antiscorbutic during the period immediately before death, showed scurvy changes in teeth, but normal picture of rib epiphyses. No. 81 and 82, on the other hand, showed certain changes in the teeth. These may be partly associated with the want of C-vitamin from which also these animals suffered for some time, and partly perhaps with the want of A-vitamin. The changes in the rib epiphyses resemble those found by DELF and TOZER with lack of A-vitamin in the food of guinea-pigs. The earlier period, during which the C-vitamin was unsufficient, necessitates a certain caution in deciding the question about the cause of these rib changes.

Series XIX.

Animals 83—86. Got 3 ccm. of fresh tomato juice (see p. 25) from October 8. Weight charts, Fig. 113. After two weeks all the animals had reached the maximum weight, grew more quiet, and their coats became rough. Somewhat later the knees were swollen and tender. Died after 39 to 43 days. At the *post-mortem* examination which was undertaken immediately or one to two days after death, they all showed the typical picture of acute scurvy, with hemorrhages in numerous muscles, loose teeth that are easily removed, swollen joints, very brittle epiphyses. No. 83 and 86 showed the above-described connective-tissue formations in the upper six rib interstices around the costochondral junctions. Histological examination as in Series V.

No. 83.

♂. White—black.

Diagnosis: Scorbut manifestus mitior.

No. 84.

♂. White—black—brown.
Liver, Fig. 75.
Diagnosis: Scorbut manifestus mitior.

No. 85.

♂. White—black—light brown.
Diagnosis: Scorbut manifestus mitior.

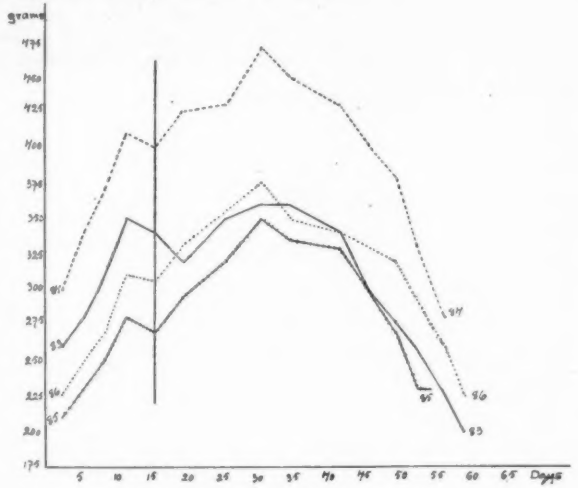


Fig. 113. Series XIX. 0.1 m. pr. d.

No. 86.

♂. White—light brown—black.
Liver, Fig. 76, 78. Liver also stained on iron.
Diagnosis: Scorbut manifestus mitior.

Conclusion for Series XIX: 3 ccm. of fresh juice from late-ripened tomatoes have shown a very inconsiderable antiscorbutic effect.

Series XX.

Animals 87—90. From October 4 they got, besides cereal and bran, unboiled milk, together 200 ccm., which they consumed.[1] After two weeks the animals grew quiet, reached the maximum weight after 19—23 days and soon showed swollen, tender joints, scurvy position of the hind-legs etc. Weight charts, Fig. 114.

No. 87.

♀. White—black—light brown.
Dead $^{10}/_{11}$, autopsied $^{12}/_{11}$. Hemorrhages around the costochondral junctions of the upper five pairs of ribs, which are all enlarged, and around

[1] The milk had been heated at 66° C. for 20 minutes and was given to the animals 24 hours later.

the swollen knees. Along the caudal edge of the fifth, right rib a connective-tissue formation obliquely backwards from the costochondral junction. Teeth loose. Epiphyses fragile. Lymph-glands on the neck swollen.

Diagnosis: Scorbut manifestus mitior. Infectio ac.

No. 88.

♀. White—light brown—black.

Dead $^{3}/_{12}$, autopsied $^{4}/_{12}$. Changes similar to No. 87, but quantitatively more developed. Hemorrhages exceedingly numerous; epiphyses very brittle. Pale masses of connective tissue (Fig. 55, 61) fill up the lst — 7th interstices on both sides between the costochondral junctions, which are swollen. Ribs stained with Weigert's fibrin stain, and besides, as also knees, spleen and liver, on iron. Jaw, Fig. 10, 11.

Diagnosis: Scorbut manifestus mitior.

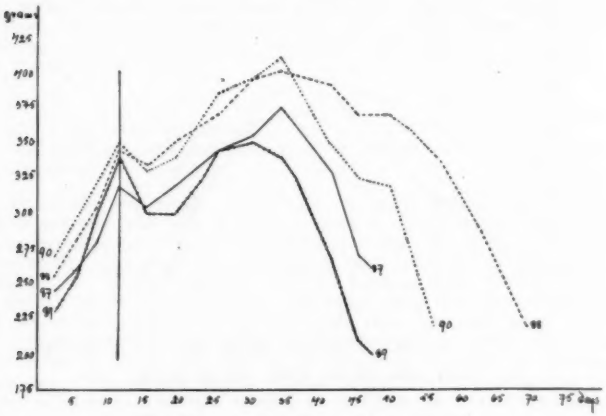


Fig. 114. Series XX. 0.1 m. pr. d.

No. 89.

♀. Black—light brown—white.

Dead $^{10}/_{11}$, autopsied $^{12}/_{11}$. Progress and findings as in No. 87.

Diagnosis: Scorbut manifestus mitior.

No. 90.

♀. White—light brown—black.

Dead and autopsied $^{19}/_{11}$. A submaxillary lymph-gland forms a large abscess. Infectious spleen. Hemorrhages around the swollen knees and the enlarged costochondral junctions. Round these on the left side from the 4th to the 7th rib, swellings of the intercostal musculature, as described above. Histological examination as in Series V.

Diagnosis: Scorbut manifestus mitior; lymphadenitis suppur. submaxillar.

Conclusion for Series XX: In this series, where the animals have been able to consume at pleasure the substance which was to be tested, the lifetime has varied considerably. It is indicated that about 100 ccm. of

milk are necessary for complete protection. The antiscorbutic value of milk, however, is highly variable, and the milk given in this experiment seems to have been relatively deficient in this respect.

Series XXI.

Animals 91, born $^{19}/_{9}$ of No. 33, and 92, born $^{7}/_{10}$ of No. 14. They got basal diet from October 28, and besides 5 ccm. of raspberry juice, bought at a pharmaceutical chemist's as »syrupus Rubi idaei 1922». The animals progressed as cases of absolute scurvy, with maximum weight after 15 and 18 days, to death in 28 and 27 days. Weight charts for Series XXI and XXII, Fig. 115.

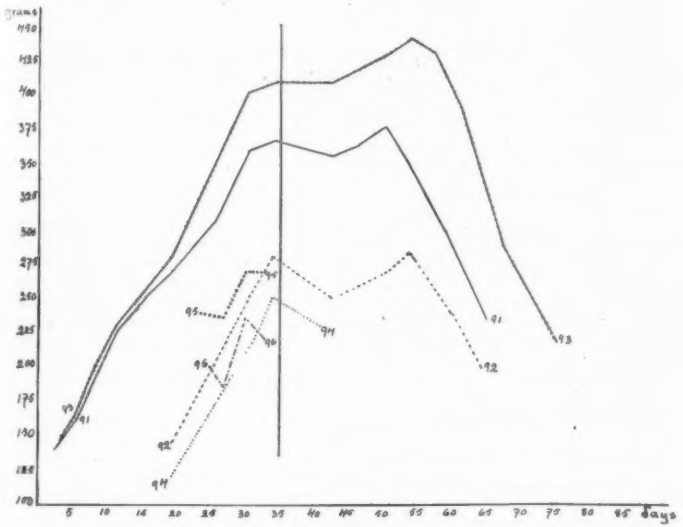


Fig. 115. Series XXI—XXII. No antiscorbutic.

No. 91.

♀. Light brown—black.
Dead $^{25}/_{11}$, autopsied $^{27}/_{11}$.
Diagnosis: Scorbut manifestus gravior.

No. 92.

♀. White—black—light brown.
Dead $^{24}/_{11}$, autopsied $^{27}/_{11}$.
Diagnosis: Scorbut manifestus gravior.

Conclusion for Series XXI: The preparation called raspberry juice has in two cases shown no antiscorbutic effect.

Series XXII.

Animals 93, born $^{9}/_{9}$ of No. 33, and 94, born $^{7}/_{10}$ of No. 14. They got from October 28 basal diet and besides 5 ccm. of black currant juice from the same pharmaceutical chemistry as the juice in Series XXI. No. 93 progressed as a case of absolute scurvy, with maximum weight after 19 days, to death in 37 days. Histological examination as in Series V. No. 94 died after six days $^{8}/_{11}$; the cause of death could not be established (overlying?)

No. 93.

♂. Light brown—black.
Dead $^{9}/_{12}$, autopsied $^{4}/_{12}$.
Diagnosis: Scorbut manifestus gravior.

No. 94.

♀. White—black.
Dead $^{3}/_{7}$, autopsied $^{5}/_{11}$. The animal had been flattened against the floor of the cage by its fellows. Nothing pathological found in different organs except what was due to this circumstance.
Diagnosis: Scorbut latens gravior. Causa mortis incerta.

Conclusion for Series XXII: The preparation called black currant juice has in one case shown no antiscorbutic effect.

Series XXIII.

Animals 95 and 96. Healthy animals, which both at the first feeding with the red whortleberry juice given in Series 4 blew it out through the nose; all their muscles relaxed and they died, one after having staggered a few steps in the cage, the other almost immediately in the hand. The feeding was not managed slowly enough. The abdomen became rapidly and strongly distended, which at the post-mortem was shown to have been caused by the ventricle being filled with gas. Microscopical examination as in Series I.

No. 95.

♀. White (albino).
Dead and autopsied $^{2}/_{8}$.
Diagnosis: Reflex death?

No. 96.

♀. White—black.
Dead and autopsied $^{2}/_{8}$. Ribs, Fig. 36.
Diagnosis: Reflex death?

Records belonging to Part II, Chapter I.

Extracts.

Case I.

Karl Albin P:n, No. 11181.
From the Hospital record: Born $^{6}/_{7}$ 1896, admitted that day.
Clinical diagnosis: $^{6}/_{7}$ 1896 conjunctivitis catarrhalis + macroglossia; $^{8}/_{9}$ icterus neonatorum; $^{13}/_{7}$ mastitis; $^{20}/_{8}$ lues suspecta; $^{9}/_{9}$ eczema faciei; $^{6}/_{11}$ gastroenterocolitis ac. + otitis med. pur.; $^{17}/_{11}$ erysipelas capitis; $^{22}/_{11}$ bronchitis bilat. ac. + otorrhoea bilat.; $^{24}/_{12}$ abscessus capitis; 1897, January: atrophia; bronchitis; $^{8}/_{2}$ morbus Barlow; $^{16}/_{3}$ mors.

Breast-fed for nearly 2 months. Then the weaning was begun and completed in 2 weeks; after that milk mixtures.

The weight increased steadily, from 3,600 grams at the birth on $^{6}/_{7}$ to 5,600 at the age of 3 months (then, $^{8}/_{10}$, dyspepsia). Then it sank uninterruptedly to 4,200 grams on $^{17}/_{12}$, and after that date rose again irregularly; during the last weeks it sank from 5,200 to 4,600 grams.

Daily records: $^{24}/_{10}$ nose-bleed; $^{22}/_{1}$ meatus audit. filled with bloody secretion; $^{28}/_{1}$ bloody discharge from nose; $^{29}/_{1}$ the gingiva over the incisors in the upper jaw imbibed with blood and swollen over each tooth not yet cut. $^{30}/_{1}$ Abundant discharge from the right ear of bloody secretion like that from the nose. $^{6}/_{2}$ Considerable edema in both legs. Bloody discharge from nose and left ear. Liver rather hard, reaches the navel plane; spleen reaches the front axillary line. Percussion area of heart from 1 cm to the left of the mammillary line to the middle of sternum. $^{8}/_{2}$ Lower parts of tibiæ and fibulæ considerably swelled and tender. $^{12}/_{2}$ Right thigh diffusely swollen. Complete immobility of both legs. No swelling of the arms which he moves a little, but slowly. Temp. about 37,5° C. $^{22}/_{2}$ Hemorrhage on the left upper lid. $^{4}/_{3}$ Periosteal swellings, most pronounced in the lower part of the right femur, the upper and lower parts of the right fibula and tibia and the lower ends of the left fibula and tibia. $^{10}/_{3}$ Died with lung symptoms.

Post-mortem on $^{10}/_{3}$. *Patho-anatomical diagnosis:* Haemorrhagiæ subperiostales, intramusculares et pulmonum + pneumonia ac. bilateralis + pachymeningitis haemorrhag. interna + hyperplasia lienis + otit. med. purul. sin.

From the post-mortem record: General complexion pale. In the tela subcutanea on the lower part of the left leg and foot a quite considerable edema. Ribs somewhat enlarged at costochondral junctions. At incision no sign of rickets is found. *Right thigh:* The musculature close to femur strongly infiltrated with blood and dark red. Periosteum raised all round by a layer of partly clotted blood, 1—5 mm. thick. Thus, a subperiosteal hemorrhage extends from the upper to the lower epiphysis. Both epiphyses had become loosened from the diaphyses. In the *right leg* mainly the same picture with fractures of both epiphyseal ends in *tibia* as well as *fibula*. A similar picture in the left thigh and leg; epiphyseal fracture is absent only in the upper part of the left fibula.

On the right and left side slight periosteal hemorrhage in *ulna* and *radius*. Joints and epiphyseal cartilages everywhere normal without any sign of rickets.

Lungs: The left upper lobe shows numerous miliary, dark red hemorrhages. Pneumonia in the whole of the left upper lobe and in smaller areas of the right upper lobe.

Liver: Slight fatty infiltration.

Microscopical examination: Left femur, lower epiphyseal line and the upper limit of right tibia display a marked picture of scurvy with low cartilage columns, »Gerüstmark» and »Trümmerfeldzone». (Detail Fig. 49 a). In the »Fugenwinkel» there is inferior bone in splinters (Fig. 49 b) and in bone columns higher up in the marrow homogeneous places (Fig. 49 c).

Epicrisis: Case of infantile scurvy, having displayed definite clinical changes in the seventh month and died of lung complication less than 2 months later. No rickets.

Case 2.

Gösta Reinhold Emanuel V-g, No. 11271.

From the Hospital record: Born $^{30}/_{9}$ 1896. Admitted $^{6}/_{10}$ 1896.

Clinical diagnosis: $^{8}/_{10}$ intertrigo, bronchitis: $^{31}/_{12}$ otorrhoea; $^{25}/_{1}$ 1897 abscessus retroaur. sin.; $^{1}/_{4}$ bronchitis; $^{22}/_{4}$ lymphadenitis; $^{22}/_{4}$ otit. med. pur.; $^{30}/_{4}$ pneumonia ac. dx.; $^{10}/_{5}$ excema capitis, $^{22}/_{6}$ bronchitis; $^{28}/_{10}$ rachitis; $^{11}/_{11}$ periostitis + perichondritis humeri et femoris; $^{19}/_{11}$ enterocolitis ac.; $^{23}/_{11}$ mors.

The infant was entirely breast-fed the first two months; from 4 months fed solely on cow's milk.

The weight increased for 5 months, till 5,700 grams. Loss in weight afterwards 1 kg. during 4 months; then again increase, 1 $^{1}/_{2}$ kg. in 3 months till 6,500 grams a month before death.

Daily records: $^{13}/_{4}$ (six months old): Craniotabes + rosary. $^{20}/_{6}$ Mellin's food, 8 tea-spoonfuls; $^{28}/_{10}$ very strongly developed rosary. Epiphyseal junctions of ankles and wrists enlarged. Occipital suture somewhat soft; $^{1}/_{11}$ tenderness of body. Crying out whenever turned over from dorsal position. Looks poorly and eats little; $^{11}/_{11}$ complexion dull, pale grey. Always lying on his back with his arms extended down his sides and his legs turned outwards, slightly bent in the hip-joints. Thighs somewhat swollen. At the slightest touching of the extremities and when moving passively, the patient moans a great deal; $^{13}/_{11}$ left arm from acromion down towards joint heavily swollen; considerable tenderness. $^{18}/_{11}$ quiet and still when left alone. The left forearm swollen at the epiphyseal junction above the wrist; tenderness. As the symptoms from the bone system increased, the patient grew steadily worse and died $^{23}/_{11}$, 14 months old. *Post-mortem* the same day.

Patho-anatomical diagnosis: Hemorrhagiæ subperiostales (morbus Barlow) + enterocolit. follicular. ac. + otit. med. bilat. + lymphadenit. chron. gland. mesenteric. + pachymeningit. hemorrh. interna + rachitis.

From the post-mortem record: Dura mater, of ordinary thickness, shows on the inside in patches a thin, mostly yellowish brown, sometimes pale, easily loosened membrane. In the lower lobe of the left lung immediately below the pleura dispersed miliary hemorrhages. Heart af ordinary size. Musculature pale. Spleen somewhat enlarged; Malpighian corpuscles somewhat enlarged. In large portions of colon transversum the solitary follicles, which are not swelled, are found to be of a dark red blood colour, darkest in the centre, lighter in the periphery. Between these portions there are others where the follicles generally are somewhat swelled, pale, and only some few show hemorrhages like those described above.

The left brachium swollen. Musculature in the upper half discoloured, pale yellowish or yellowish brown. Periosteum on left humerus loosened by a hemorrhage. The left upper humeral epiphysis separated from the diaphysis; a layer of yellow-tinged tissue, about 2 mm. thick, sticks to the epiphysis. The right femur only shows a somewhat looser connection between epiphysis and diaphysis in the upper part, while the left femur and right humerus show pictures similar to those of the left humerus (muscle discolouring, fracture of the diaphysis close to the upper epiphysis, subperiosteal hemorrhage). Hemorrhage like this is also seen on ulna and radius of both sides.

The ribs are considerably enlarged everywhere at the junction between cartilage and bone. At incision the cartilage proliferation zone is found to be a great deal wider than normally, generally 3—4 mm. wide. The calcification zone is exceedingly irregular. Adjoining this there is a yellowish

zone about 1 mm. wide of a soft tissue in which the bone is loosened from the cartilage. Under the periosteum, which evidently is slightly raised, a thin layer of dark red, not clotted blood extends 1—2 cm. from the junction of the cartilage and bone.

Microscopical examination. Cut sections were made of the lower left femoral epiphysis and a large number of ribs, *not decalcified;* the specimens were treated according to v. RECKLINGHAUSEN with carmalum and aluminated glycerin.

Left femur: The epiphysis has narrow bone columns, in the large majority normal injection. *In certain columns only the corpuscles injected, without canals.* In another series next to the epiphysis are seen 1) narrow columns with complete injection, 2) colourless columns with injection of corpuscles, but no canals, 3) colourless columns without any trace of injection, and 4) some few red-coloured columns without injection. In the marrow sparse cells and hemorrhages. (Note: When staining sections from the same place with hematoxylin and carmin, the majority of the columns are found to become blue-coloured, only a few tender columns red-coloured, in this manner proving that the bone columns are prevailingly calciferous, and only exceptionally osteoid.)

Rib. 1, not decalcified, treated according to v. Recklinghausen. In the parts next to the cartilage the bone columns are colourless, glossy, and there are no injected corpuscles or canaliculi to be seen in them, or else only small corpuscles without canaliculi. Farther away from the cartilage, however, injection of the bone column is found, in some places throughout the column, in other places there is injection in the central parts but round those a narrow zone, uncoloured and glossy, without injection of corpuscles or only of small, dwarfed ones without canaliculi. Other sections from the same rib show: 1) Next to the cartilage a narrow zone, in which there are numerous tender columns of a red-coloured tissue, which in some places seems to be quite homogeneous (remaining rests of the hyaline middle substance of the cartilage), but for the most part shows a structure of osteoid tissue *without* injection of corpuscles. In places there is in the centre a more deeply red-coloured tissue of hyaline nature and outside this a narrow zone of osteoid tissue (rest of hyaline cartilage surrounded by osteoid tissue). All these columns lie irregularly scattered, not parallel with the longitudinal axis of the bone. The bone marrow in this zone is fairly abundant in cells, and there have been both fresh and earlier hemorrhages. 2) Then a zone, in which the bone columns are very tender, not coloured, evidently calcified, but without injection of corpuscles. 3) Then again a zone with distinct injection of the bone canals.

Rib. 2. a. Cut section, hematoxylin-carmin.

The cartilage proliferation zone wider than normally. The calcification zone is narrow, and not seen in the most peripheral parts. Next to this is a zone of numerous small detached pieces of calcified cartilage tissue together with some columns of osteoid tissue (red-coloured) and some of calcified bone tissue (blue-coloured).

b. not decalcified, treated according to v. Recklinghausen.

In the zone next to the cartilage, scattered narrow, glossy columns, which are uncoloured and do not show any injection with carbon dioxid, or only of a few corpuscles without canaliculi. This zone evidently extends higher on the outward surface than on the pleural side.

Epicrisis. Case of infantile scurvy, dying at the age of 14 months, having displayed definite clinical symptoms during the last months. Rickets.

Case 3.

Fredrik Albert, born $^{6}/_{12}$ 1896. Admitted $^{9}/_{12}$ 1896.

The weaning began $^{1}/_{2}$ and was completed within 2 months. From $^{16}/_{2}$ Mellin's food was administered, 3 tea-spoonfuls, from $^{10}/_{5}$ raised to 8 tea-spoonfuls. The weight increased during the first 4 months to 5,000 grams but afterwards kept to about 5 kg. (4.6—5.4) until death at the age of 10 months.

Clinical diagnosis: $^{28}/_{12}$. 96 conjunctivitis catarrh. + dyspepsia; $^{1}/_{3}$. 97 otitis; $^{29}/_{3}$ bronchitis; $^{10}/_{5}$ gastroenteritis; $^{13}/_{6}$ otitis; $^{28}/_{8}$ pneumonia ac. sin.; $^{6}/_{10}$ pneumonia ac. sin.; $^{7}/_{10}$ mors.

The daily records have not been found. The clinical diagnosis was: pneumonia ac. + septicemia.

Post-mortem examination on $^{9}/_{10}$.

Patho-anatomical diagnosis: Pneumonia ac. bilat. + splenitis ac. levis + nephrit. ac. parenchym. levis + colit. follicular. chron. et ac. + *hemorrhagia subperiostal. femor. ambor.* + otit. med. bilat.

From the post-mortem record: »The corpse is pale. In the upper side of the feet rather profuse edema. Both thighs quite considerably swollen. Musculature in the outer layers of pale flesh-colour, in the deeper ones discoloured, pale grey-red or of a dirty yellow, always having a gelatinous, transparent look. In a few small places in the musculature are seen slight hemorrhages. The periosteum on both sides raised from femur by a layer of blood, 1—5 cm. thick.» —

Microscopical examination. Series of sections from left femur, both from the two epiphysis ends and from different parts of the diaphysis. Staining: htx-eosin, htx-carmin and v. Gieson. Cut sections from the same places, prepared according to v. Recklinghausen.

By way of example some of the sections from the upper epiphysis end are here described.

1. Cut section, carmalum (v. R.).

Tender bone columns, the large majority showing complete injection. In a smaller number, incomplete or hardly any injection in the uncouloured columns. Some few columns are red-coloured and at the same time without injection (osteoid).

2. Cut section, same treatment.

Tender bone columns, generally showing injected bone corpuscles and bone canals throughout the column, but nearer the epiphysis not all the columns are found to be injected; sometimes merely scattered black corpuscles without canaliculi; sometimes a centre which is normal and outside that a narrow zone of white glossy colour *without* injected corpuscles.

3. Detail of section showing (Fig. 50) an old bone bridge, on the epiphyseal end of which there is an abundant layer of homogeneous, eosinophile bone, reaching the cartilage.

The sections in the upper, lower and middle parts of the left thigh show everywhere an exceedingly strong atrophy of the muscular fibres (Fig. 65 a and b).

Epicrisis. A 10 months' child, who since the age of 4 months was entirely fed on milk mixtures and during all this time has kept the same weight and in whom the *post-mortem* examination revealed pronounced scurvy.

Case 4.

Judit Teresia L-l, born $^{8}/_{6}$ 1899.
Admitted $^{10}/_{6}$ 1899.
Clinical diagnosis: $^{21}/_{8}$ Lues hereditaria; $^{8}/_{11}$ ulcus frenul. linguae; $^{13}/_{11}$ bronchitis; died $^{15}/_{11}$ 1899.

Was from her birth fed with cow's milk mixtures. Was given milk powder from $^{15}/_{8}$. Gained weight slowly from 2,920 grams on the day of admittance to 3,790 at 3 months, afterwards went down to 3,380 the day before her death, at the age of 5 months.

Treated with Hg per os after $^{1}/_{9}$.

The first of the daily records which is indicative of scurvy is of $^{14}/_{11}$ (the day before death) and says: Swellings on the thighs. The soft parts are firm to the touch and infiltrated. Swellings on the upper side of both feet. Eats very little, fretful and whimpering.

Died $^{15}/_{11}$, *post-mortem* examination $^{16}/_{11}$.

Patho-anatomical diagnosis: Hemorrhagiæ subperiostales (morbus Barlow) + pneumonia lobularis dx. + hyperplasia lienis.

Extracts from the post-mortem record: On the left thigh the musculature (mostly cruralis, but also vastus ext. et int.) is discoloured, of a greyish yellow, sometimes a little yellowish brown, and also shows small freshly occurred hemorrhages. Round the whole femur below the periosteum a layer of clotted blood, 1—3 mm. thick.

The lower right femoral epiphysis shows the cartilage proliferation zone about 2 mm. wide; the calcification zone is just above 1 mm. wide, greyish yellow, generally straight, but in some places uneven. The bone marrow next to this zone is changed into a dark red and muddy pulp.

Around the lower ends of both tibiæ and the right radius subperiosteal hemorrhages. The upper epiphyseal line of tibia is similar to the lower one of femur.

The ribs show on the pleural side, both at the posterior and anterior epiphyseal junctions, fresh hemorrhages below the periosteum. On the section at the junction of cartilage and bone, the cartilage proliferation zone is now 1 mm., now 1/2 mm. wide, yellowish, on the whole even towards the cartilage but with small notches.

Microscopical examination. Staining: hematoxylin-eosin, alum. hematoxylin — v. Gieson, of the two femores, tibiæ and fibulæ, as well at the upper and lower epiphyseal lines as in the middle of the diaphysis; also the anterior and posterior epiphyseal junctions of two ribs.

The upper end of left femur: frame-work marrow 1 mm. high. Inferior bone covers the old bone bridges in the »Trümmerfeldzone». It shows bone canals but hardly any other structure.

The upper end of left fibula: no cartilage trabeculæ, the bone formation seems altogether arrested. In the musculature, which is highly atrophic, pictures of regeneration.

Ribs, posterior end: The bone columns, which are lying across in the frame-work marrow of 3 mm. width, are joined to the cartilage through a system of columns of more homogeneous bone. Round all the bone columns a thin zone of red tissue (osteoid) and spool-shaped osteoblasts (Fig. 5). In the »Fugenwinkel» hyaline bulky bone.

Epicrisis. Scurvy in a child of 5 months (the mother syphilitic), from the birth fed first with cow's milk mixtures and then with milk powder.

Records, belonging to Part IV, Chapter II.

Extracts.

Series XXIV.

Animals 97—103, 183, control animals on complete dietary. Weight charts, Fig. 116. No. 97 died of an acute infection, the others were chloroformed after 105 days, July 3rd, and autopsied immediately. Histological examination as in Series V.

No. 97.

♀. Light brown—black.

Increased during 50 days normally, then decreased during 5, with symptoms of panting respiration. Died 11/8 23. Autopsied 12/8. Histological examination as in Series V, and of lungs, shows an infection spleen, numerous foci in the lungs, where the alveoli are filled out with red blood-corpuscles, mono- and polynucleate cells.

Diagnosis: No scurvy. Bronchopneumonia ac.

No. 98.

♂. White (albino).
Showed during some weeks in May a hairless spot on the back, big as a sixpenny piece, which healed spontaneously.
Liver 27.5 grams. Spleen 1.2 gram.
Diagnosis: No scurvy.

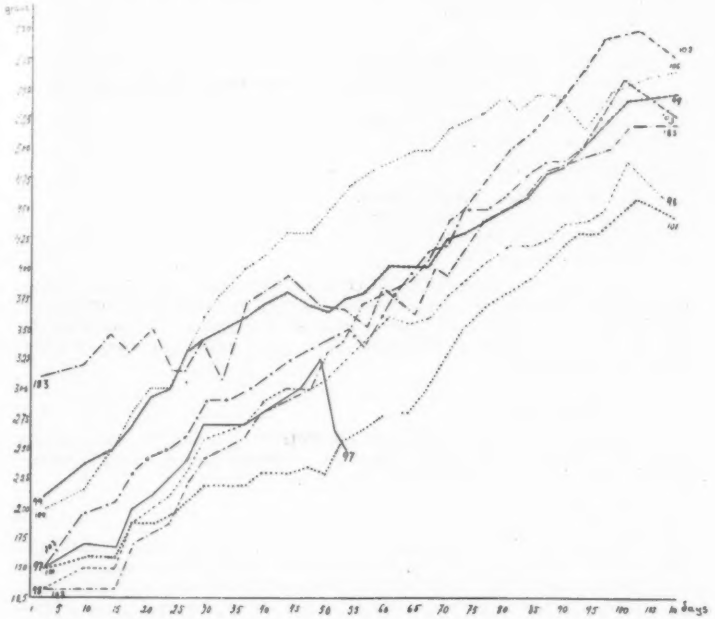


Fig. 116. Series XXIV. Complete dietary.

No. 99.

♀. Brown—white—black.
Showed at the *post-mortem* 3 feti, 3 cm. from vertex to coccyx, two in the right uterine horn, one in the left.
Liver 28.2 grams, spleen 0.75 gram.
Diagnosis: No scurvy.

No. 100.

♀. Brown—white—black.
Liver 31.3 grams, spleen 1.1 gram.
Diagnosis: No scurvy.

No. 101.

♂. White—brown—black.

After an unsatisfactory increase in weight during a month, it was noted $^{23}/_{5}$, that the animal showed a tendency of sinistroflexion of the head. This symptom disappeared again after two weeks. In the beginning of May the animal also had a hairless spot on one flank which healed spontaneously after a short time. Liver 25.1 grams, spleen 1 gram. Histologically normal picture. Kidneys not examined.

Diagnosis: No scurvy.

No. 102.

♂. Black—light brown—white.

Showed at the end of May during a short time a hairless spot on the trunk, healing spontaneously.

Liver 31.1 grams, spleen 1 gram.

Diagnosis: No scurvy.

No. 103.

♀. White—light brown—black.

Liver 27 grams, spleen 1.1 gram.

Diagnosis: No scurvy.

No. 183: see p. 232.

Conclusion for Series XXIV: Of 8 animals that were given complete dietary, one died of pneumonia, the others lived till they were killed at the conclusion of the experiment, or more than 3 months. Neither clinically, nor at the *post-mortem* or the histological examination any sign of scurvy could be discovered.

Series XXV.

Animals 104—111. Had complete dietary of oats and bran, unboiled milk, and swedes *ad lib.* from March 20. Infected March 29 with tubercle bacilli (see p. 151). Weight charts, Fig. 117.

No. 104.

♂. White—yellow.

Chloroformed $^{30}/_{6}$, autopsied the same day. Strong, fat animal. Hair firmly fixed. No sign of scurvy. In the adductors of the right thigh a cavity, less than almond-sized, with uneven, hard-rinded walls several mms. thick, containing a turbid liquid with necrotic strips. Lphgl. ing. dx., big as a brown bean, shows a miliary abscess cavity surrounded by a distinct capsule, $^{1}/_{2}$ mm. thick, with columns that penetrate into the cavity. In other lymphglands a homogeneous swelling. Spleen 1.7 gram. Liver 38.2 grams. Histological examination according to Series V shows no sign of scurvy. *Liver:* Foci and strands of granulation tissue, of epitheloid cells, fibroblasts, lymphocytes and other round cells, young liver cell columns. In this tissue there are seen Langhans' giant cells and tubercle bacilli at intervals. From some vessels strong strands of connective tissue. Hardly any fat. In the *spleen* large areas where only reticular cells are seen. Numerous giant cells of Langhans' type and others; fibroblasts very few. In the lphgl. submax. there are small foci of epitheloid cells and giant cells, some of Langhans' type, some more irregular, and tubercle bacilli. Section through the primary focus shows necroses farthest in. Outside these a wide layer of connective tissue, at intervals a Langhans' giant cell and numerous calcium lumps; also the protoplasm of the giant cells is calcified. This connective tissue is arranged as a capsule around necroses and shows strong collagen fibrils. In a lymphgland lying

next to the focus, the centre shows a necrotic focus where inside almost every cell-outline there is a dark grain (calcium); outside that a zone of large calcium lumps; around that a tissue of fibroblasts and a few epitheloid cells, and rests of lymphatic tissue. *Lungs:* In lymph nodules a few epitheloid cells and Langhans' giant cells.

Diagnosis: No scurvy. Tbc prim., musculor., lmphgl. regional. et aliar., lienis, hepatis, pulmon.

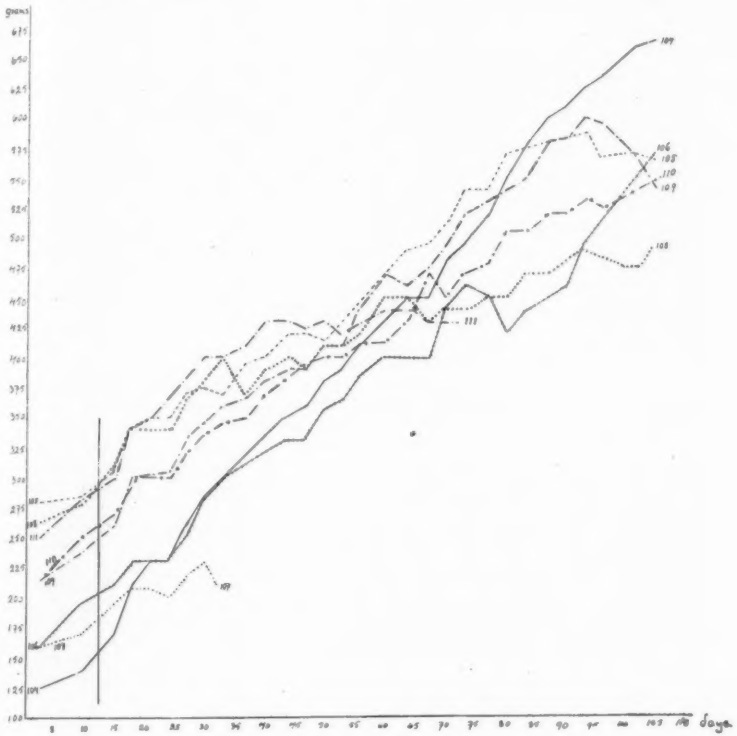


Fig. 117. Series XXV. Complete dietary. All animals tubercular.

No. 105.

♂. White—black—brown.

Did not increase in weight during the last three weeks. Chloroformed and autopsied $^{30}/_{6}$; muscular, fat animal. In the adductors of the right thigh an extensive *focus*, following the muscle interstices in different ducts, bordered by a rind formation, hard as cartilage, with caseous contents. Regional *lymphglands* at both knees, the right groin and at the entrance to the pelvis, of the

same hardness, with miliary caseous foci. The largest of the lumbar glands, large as a brown bean, shows three such distinctly separate foci. *Liver* 39.0 grams, filled with miliary greyish white granulations. *Spleen* 4.1 grams, with prominent follicles. *Lungs* filled with miliary greyish white hard grains. Lymphglands in the lung hilus also fibrously changed; very hard. Histological examination as in No. 104 with similar pictures.

Diagnosis: No scurvy. Tbc primar., musculor., lmphgl. regional. et aliar., lienis, hepatis, pulmon.

No. 106.

♀. White—light brown—black.

Seemed vigorous till death. Through an accident broken both hindlegs $^{23}/_{5}$. Chloroformed and autopsied $^{30}/_{6}$. No sign of scurvy. In the adductors of the right thigh caseous abscesses following the intermuscular connective tissue upwards to the inguen and downwards below the knee, bordered by rind-like connective tissue. Tibiæ of both hindlegs broken, bone edges united by abundant callus. Lymphogl. ing. dx. miliary, wholly caseous, lmphgl. genu on both sides fibrously changed. Liver 34.3 grams, spleen 1.2 gram. In the middle lobe of the right lung a lentil-sized, grey gelatinous-looking round nodule, fibrous under the knife. Lymph-glands for the rest of ordinary consistence, except in the lung hilus, where they are also hard. Histological examination as in No. 104.

Diagnosis: No scurvy. Tbc primar. musculor., lmphgl. regional. et pulmon., lienis, hepatis et pulmon.

No. 107.

♀. Light brown—white.

Seemed well till the beginning of April. Increase in weight bad during the last two weeks. Died $^{19}/_{4}$. Autopsied $^{21}/_{4}$: hair does not come off. Teeth somewhat loose. Incisors chalky. Ribs normal. Joints without remark. General brittleness of bones. No hemorrhages. Claw-bed of the paw on the right fore-leg blue-violet. Hyperemia of the extremity. Right axillary lymph-gland strongly hyperemic. Tests of bacilli negative. Mucous membrane of larynx wrinkled, in trachea pale. Lungs: 0. Liver 10.6 grams, spleen 0.55 gram. No macroscopic signs of tuberculosis. Histological examination as in No. 104. Teeth show a totally normal picture, even of the odontoblast layer. Section of the right paw shows changes principally in connective-tissue and joint-cartilage. The connective-tissue has abundant thin-walled vessels. For the rest there is in some places the picture of an incipient necrosis. The joint-cartilage has an uneven surface, and some fibrous portions are seen in the joint which also contains a number of erythrocytes. In the musculature of the right thigh there is a small necrosis surrounded by fibrous connective-tissue, in which there are seen some few Langhans' giant cells. The arteries of the extremities not examined.

Diagnosis: No scurvy. Tbc localis musculor.

No. 108.

♂. Light brown—black.

Less satisfactory increase in weight during the last five weeks. Chloroformed and autopsied $^{30}/_{6}$: No sign of scurvy. The purulent local focus follows the interstices of the adductors to the connections. The boundary surface granulous, bright red. Lymph-glands in right knee small, fibrous, with calcium scrapings. In the inguen a pea-sized lymph-gland with three miliary abscesses. Other lymph-glands homogeneous, swollen. Liver 46.2 grams, spleen 29.2 grams, considerably increased in volume, the former filled with miliary grains, the latter mottled, very full of blood. The lungs show

numerous miliary granulations with hyperemic zone. Histological examination as in No. 104. Examination on amyloid in spleen negative. Spleen: large necroses with connective-tissue. For the rest as No. 104.

Diagnosis: No scurvy. Tbc primar.; lmphgl. regional., lienis, hepatis, pulmon.

No. 109.

♀. White—black—light brown.

Decreased in weight during the last twelve days. Chloroformed $^{30}/_{6}$ and autopsied $^{2}/_{7}$: Fat animal No sign of scurvy. In the uterine horns 3 feti, 3.5 cm. from vertex to coccyx. Feti and placenta show no signs of tuberculosis. Local focus in the muscles of the right thigh very small, of 5 mm. diameter, very hard-rinded, with an abscess in the centre, big as a pin's head. Lymph-glands at right knee, inguen and pelvis enlarged, all through rind-like and fibrous, each with one to four small purulent foci, surrounded by a caseous demarcation zone. The connective-tissue so hard that it grates against the knife. *Spleen* very voluminous, 5 × 3.5 × 3.5 cm., 16.1 grams, shows yellow foci varying in size and surrounded by a hemorrhagic border zone. *Liver* granular on surface, very hard. *Lungs* filled with miliary and somewhat larger granulations, yellow or grey, surrounded by a hyperemic zone. Five lymph-glands in hilus rindlike and fibrous, one with a small abscess. Histological examination as in No. 104. Liver: the regenerative strands occupy the larger part of the liver, are of a markedly fibrous character, while liver columns, epitheloid cells, Langhans' giant cells and round cells are somewhat less conspicuous. Tuberculous granulation tissue in spleen, lymph-glands, lungs, shows fibroblasts dominating among epitheloid cells, Langhans' giant cells, lymphocytes, calcium grains and tubercle bacilli. Granulation foci in the marrow of two ribs.

Diagnosis: No scurvy. Tbc primar. lmphgl. regional.; lienis, hepatis, pulmon.; lmphgl hil. pulmon.; costar.

No. 110.

♂. Yellow—white.

Increased uninterruptedly in weight, till it was killed by chloroform $^{30}/_{6}$. Autopsied $^{2}/_{7}$: Fat animal. No sign of scurvy. In the muscles of the right thigh there is an extensive rindlike connective-tissue, in which a miliary abscess is found. Lphgl. genu bilat. enlarged rind-like, with 0—5 small purulent foci. Lphgl. ing. not so hard; smaller. Lumbar lymph-glands like the knee glands. Some lymph-glands in the lung hilus are harder still. One of them has a small abscess. Lungs, spleen and liver sparingly filled with yellow-grey granulations, somewhat more than miliary in size, surrounded by a hyperemic zone. Liver 49.7 grams, spleen 4.1 grams. Histological examination shows pictures like those in No. 104.

Diagnosis: No scurvy. Tbc primar., lmphgl. regional., lienis, hepatis, pulmon., lmphgl. hil. pulmon.

No. 111.

♂. Black—brown—white.

After a standstill in weight during a month, the animal died $^{27}/_{8}$. Autopsied $^{30}/_{8}$. Fat animal. No sign of scurvy or acute infection. In the musculature of the right thigh an almond-sized abscess, surrounded by very thick connective-tissue rinds. The lymph-gland of the right inguen miliary in size, caseously changed all through. All lymph-glands homogeneously swollen. Spleen 17.7 grams, liver 36 grams. In the spleen, small white submiliary foci. Histological examination like No. 104 gives similar pictures.

Diagnosis: No scurvy. Tbc primar., lmphgl. regional., lienis, hepatis, pulmon., costar. duo.

Conclusion for Series XXV. The series shows that the stock of tubercle bacilli that has been used must be indicated as having rather small virulence for guinea-pigs. One died of an unascertained illness after 27 days and only at the microscopical examination the primary focus was found in the musculature. Six of the animals lived till they were killed after 102 days. The tuberculosis was then general. Common to all the cases is the fibrous character of the connective tissue which is seen in and around the tuberuculous foci in muscle, lymph-glands and parenchymatous organs. The primary focus in the musculature is bordered by rinds of connective-tissue, more than a millimeter thick, which, however, often contain epitheloid cells and Langhans' giant cells. The regional lymph-glands are for the most part changed into hard fibrous tissue, in which there are often seen one or several small abscesses. Between them strong connective-tissue septa penetrate.

Series XXVI.

Animals 112—119. Of these No. 116—119 were infected $^{29}/_3$ with tuberculosis. All were kept on basal diet without addition from this date and died within 36 days. Weight charts, Fig. 118.

No. 112.

♂. White—light brown.
Died $^{26}/_4$, autopsied $^{27}/_4$. No sign of infection. Hemorrhages around knees, wrists and most ribs. The costochondral junctions enlarged, around almost all of them mouldings of connective-tissue swellings, such as described above. Teeth can easily be removed. Increased fragility of epiphyses not so much of diaphyses. Jaw brittle. Liver 12 grams, spleen 0.22 gram. Histological examination shows pictures like those in No. 5.
Diagnosis: Scorbut manifestus gravior.

No. 113.

♂. White—yellow—black.
Died $^{17}/_4$. Autopsied $^{18}/_4$. Teeth loose. Epiphyses of the long bones easily breaking. Hemorrhages around the swollen costochondral junctions, which show the white line, and around the swollen knees. An ulceration on the left fore-paw, corresponding to metacarpus, with subcutis as bottom. Lmphgl. axillaris bright pink. Histological examinaton shows in different organs scorbutic changes as in No. 5. Kidney, Fig. 87. Heart, Fig. 67. In muscles, the ulceration on metacarpus, in spleen, liver, lung, tubercle bacilli were looked for with negative result.
Diagnosis: Scorbut manifestus gravior.

No. 114.

♂. Black—white.
Dead after one day, on $^{30}/_3$. Autopsied $^{5}/_4$: body in state of decomposition.
Diagnosis: Infectio?

No. 115.

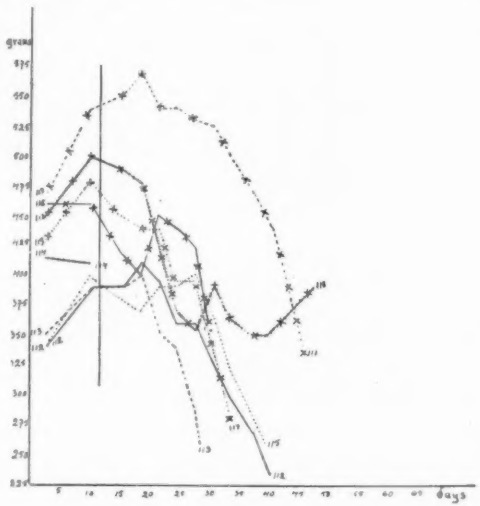
♂. Black—white—yellow.
Died, with picture of scurvy, $^{27}/_4$. *Post-mortem* examination on $^{29}/_4$ and histological examination show similar changes as in No. 112.
Diagnosis: Scorbut manifestus gravior.

No. 116.

♂. White (albino).
Died with scurvy symptoms $^{16}/_4$, autopsied $^{18}/_4$. Hair easily loosening.

Large hemorrhages around right knee and the six upper pairs of ribs on the right side. These costochondral junctions swollen on both sides. Teeth can easily be removed. Upper jaw brittle. Lmphgl. inguin. dx., paratracheal, and submaxillar, slightly homogeneously swollen. Liver 23.5 grams, spleen 0.6 gram. Histological examination of 10 ribs shows absence of ordered cartilage column layer and of ossification in the light-coloured frame-work marrow. In the *musculature of the right thigh* there is a necrotizing granulation tissue, and around that an extraordinarily vascular zone. In the vicinity there are numerous small necroses of muscular fibres with embedded calcium lumps. Nowhere any connective tissue is seen to bound or grow through the necrotic foci. In the *spleen* the lymphoid tissue is to a large extent replaced by epitheloid cells. Tubercle bacilli are very numerous. No amyloid. *Liver* shows abundant fat, and atrophy. Small foci of epitheloid cells, fibroblasts, giant cells of undecided type, tubercle bacilli. In lmphgl. submaxillar. hyperemia, epitheloid cells, tubercle bacilli. In the bronchi exudate. Adrenals, p. 102.

Diagnosis: Scorbut manifestus gravior. Tbc. muscul. primar., lienis, hepatis, lmphgl. submaxillar. Bronchitis.



The lines with ×× represent tubercular animals.

Fig. 118. Series XXVI. No antiscorbutic.

No. 117.

♀. White—black.

Progress to death $^1/_5$. The findings at the *post-mortem* examination $^3/_5$ and at the histological examination resemble the cases of severest absolute scurvy, that are described above. Small quantity of liquid in abdomen. Peritoneum parietale et viscerale thickened, not glossy. Liver and spleen with deposits around lower edge or pole. In the descending part of duodenum,

a small irregular sore of the mucous membrane and to the bottom of this sore a white-gray lymph-gland adheres. Lymph-glands of right knee and groin wholly caseous. Lumbar glands show caseous formation of a miliary focus in one pole. Histological examination shows pictures similar to those in No. 116 concerning primary focus, spleen, liver, lung. In regional lymph-glands necroses, which show numerous lymphocyte shadows, and very numerous tubercle bacilli. No distinct newly-formed connective tissue. Duodenal gland with large necrotic foci without specific character, with numerous tubercle bacilli.

Diagnosis: Scorbut manifestus gravior. Tbc muscul. primar., lmphgl. regional., lienis, hepatis, pulmon. Bronchitis. Ulcus duodeni. Peritonitis.

No. 118.

♀. White—black—yellow.

Eating and drinking with appetite to the last. Died and was autopsied $^{4}/_{5}$. Hair loosening, though not so easily as otherwise in scurvy. Teeth everywhere loose. In the lower jaw they are easily lifted out. Only certain of the costochondral junctions are enlarged in any considerable degree (3, 4 and 11 sin.). Hemorrhage around both knees. Upper tibia epiphyses extremely brittle. Upper jaw not brittle. Liver 15.4 grams. A bean-sized caseous lymph-gland in the liver hilus. Lungs filled with a large number of miliary, white-grey foci, caseous in the centre. In the right groin a bean-sized lymph-gland, in the pelvis lentil-sized glands, partially caseous. In the lymph-glands of the lung hilus, bean-sized, partially caseous foci. In lmphgl. submaxillar. small white foci. In the inner part of the musculature in the right thigh a hazelnut-sized, caseous abscess cavity, without macroscopical capsular formation. Histological examination as in No. 116.

Diagnosis: Scorbut manifestus gravior. Tbc primar. musculor., lmphgl. regional., lienis, hepatis, pulmon. lphgl. divers.

No. 119.

♂. Light brown—white—black.

Progress to death $^{22}/_{4}$, findings at the *post-mortem* examination $^{23}/_{4}$ and histological examination shows picture of pronounced scurvy. Also with regard to the tubercular changes in muscle, regional lymph-glands, spleen and liver, No. 119 resembles No. 116 and 117.

Liver 19.5 grams, Spleen 2.2 grams.

Diagnosis: Scorbut manifestus gravior. Tbc primar. musculor., lmphgl. regional., lienis, hepatis, lmphgl. hilus pulmon.

Conclusion for Series XXVI: Neither in the primary muscle-foci, in the regional glands, spleen or liver, nor in other affected organs there is any tendency seen of reactive connective-tissue, macro- or microscopically.

Series XXVII.

Animals 120—127. No. 124—127 were infected with tuberculosis. The animals were given basal diet and besides 0.3 ccm. of preserved orange juice (0.1 m. pr. d.). Weight charts, Fig. 119.

No. 120.

♀. White—light brown—black.

Died $^{12}/_{4}$ without having shown scurvy symptoms. Autopsied the same day. No certain changes to be observed at the *post-mortem* examination. Liver 18.6 grams. Spleen 0.7 gram. Histological examination as in No. 5.

Diagnosis: Scorbut latens extensus. Infectio?

No. 121. Black—white.

Was found lying with its head over the brim of the milk basin and its nose in the milk, $^{23}/_{4}$. Autopsied $^{25}/_{4}$. Hair easily loosening. Teeth firm; knees swollen, ribs slightly enlarged in costochondral junctions. No hemorrhages. Lymph-glands of upper jaw nearly as big as brown beans. Liver 8.0 grams, spleen 0.4 grams. Histological examination as in No. 5, and besides kidney and adrenal. Spleen, Fig. 84. Adrenal, Fig. 93.

Diagnosis: Scorbut manifestus mitior. Infectio.

No. 122. Yellow—grey.

Progress to death $^{10}/_{5}$; findings at *post-mortem* examination $^{12}/_{5}$ and histological examination similar to those in No. 5. Spleen 0.5 gram. Liver 13.7 grams. Tooth, Fig. 22.

Diagnosis: Scorbut manifestus mitior.

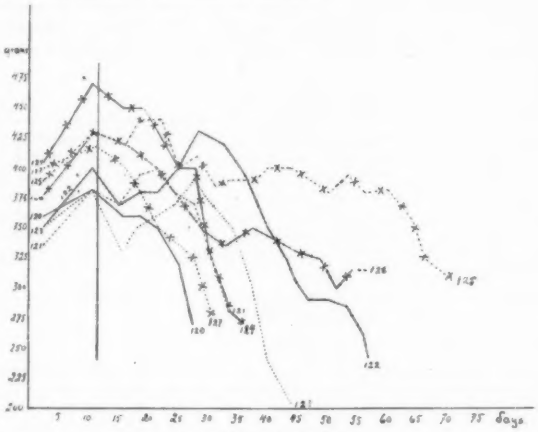


Fig. 119. Series XXVII. 0.1 m. pr. d.

No. 123. Black—white—brown.

Dead and autopsied $^{30}/_{4}$. Progress, findings at *post-mortem* and histological examinations similar to those in No. 5. Liver 10.7 grams, spleen 0.35 gram. Swelling and reddening of the mucous membrane in larynx and trachea.

Diagnosis: Scorbut manifestus mitior. Laryngo-tracheitis.

No. 124.

♂. Black—white.

Dead and autopsied $^{21}/_{4}$: Lean animal. Teeth loose, can be removed with some difficulty. The epiphyses of the long bones brittle. Upper jaw brittle. Costochondral junctions and knees swollen. Hemorrhages in the rib interstices and around right knee. Necrosis focus in thigh musculature without distinct capsule. Lymph-gland of the right groin shows small caseous foci. Spleen 0.9 gram, filled with granulations of the size of a pin's head. Liver 15.9 grams. Histological examination shows the primary focus in the musculature bordered by a wall of epitheloid cells, among which some tuberculous foci

of lymphoid cells. No connective tissue (Plate IV). Also with regard to lymph-glands, liver, spleen, the pictures are similar to those shown in No. 116 and 117.

Diagnosis: Scorbut manifestus mitior. Tbc primar. musculor., lmphgl. regional., lienis, hepatis, lmphgl. divers.

No. 125. Black—white—brown.

Died $^{27}/_{5}$, autopsied $^{30}/_{5}$. In trachea and large bronchi mucous phlegm. No hemorrhage except in the musculature of the right thigh, where it is very extensive. Teeth in the lower jaw loose. Epiphyses brittle, diaphyses not. The costochondral junctions of the ribs enlarged; some (C 6, 7, 8 sin.) surrounded by connective-tissue formations. Lymph-glands everywhere homogeneously swollen. In both groins and at right knee they are pea-sized, caseous. In a pelvis gland a pre-caseous focus. Histological examination similar to that in No. 116 and 117.

Diagnosis: Scorbut manifestus mitior. Tbc primar. musculor., lphgl. regional., lienis, hepatis, pulmon., lmphgl. divers. Tracheobronchitis, pneumoniae.

No. 126. Light brown—white—black.

Dead and autopsied $^{11}/_{5}$. Progress, *post-mortem* examination and histological pictures similar to those in No. 125. On $^{6}/_{5}$ there was observed round the left eye a small region, hairless, covered with bloody crustæ, which remained till death. No certain hemorrhage for the rest. Spleen 3.2 grams. Liver 21.8 grams. In regional lymph-glands necroses which occupy the largest part of the gland, with small calcium lumps in the centre. No distinct new connective tissue. Hyperemia of periganglionar capsule. (Plate VI). In the mucous membrane of the bladder wall a necrosis, in the wall of which there are seen bacilli looking like tubercle bacilli.

Diagnosis: Scorbut manifestus mitior. Tbc primar. musc., lmphgl. regional., lienis, hepatis, vesicae urinae.

No. 127. White—brown—black.

Dead $^{15}/_{4}$, autopsied $^{16}/_{4}$. Knees are somewhat swollen, are fractured spontaneously when taken out. Hemorrhages in muscles above right knee. The costochondral junctions slightly swollen. Teeth of lower jaw somewhat loose. Lymph-glands at right knee and tracheal lymph-glands homogeneously swollen. The middle lobe of left lung pneumonic in its upper region. Liver 20.4 grams, spleen 0.4 gram. Histological examination of 12 ribs, spleen, liver, focus in thigh musculature, gives pictures similar to those in No. 116. The alveoli of left lung in the above-mentioned region filled with red blood-corpuscles, fibrin and diplococci. In bronchi also exudate of different cells.

Diagnosis: Scorbut manifestus mitior. Tbc primar. muscul., lmphgl. regional., lienis, hepatis. Broncho-pneumonia ac.

Conclusion for Series XXVII: Hardly in any place the tuberculous foci in different organs show a connective tissue, which appears as having to be considered reactive.

Series XXVIII.]

Animals 128—134. No. 132—134 were infected with tuberculosis. The animals had basal diet and besides each 0.6 ccm. of preserved orange juice (0.2 m. pr. d.). Weight charts, Fig. 120.

No. 128.

♀. White—light brown—black.

Dead and autopsied $^{13}/_{4}$. Hemorrhages in subcutis around both knees.

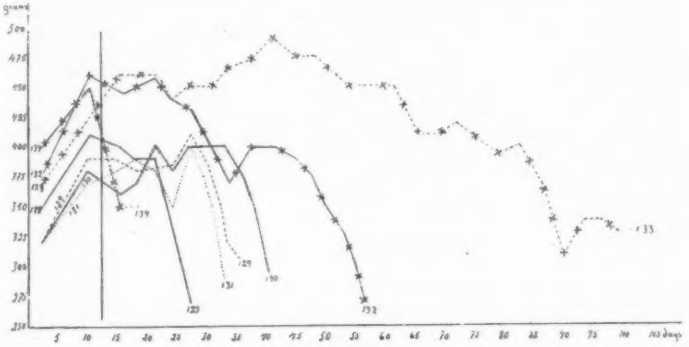
Otherwise no macroscopical signs of scurvy. The large intestine filled with thin liquid contents. Hyperemia and hemorrhage in its lymph nodules (Peyer's plaques). Corresponding lymph-glands in the mesentery bean-sized, hyperemic. Histological examination of the mentioned organs, 12 ribs, liver (18.9 grams, spleen (1.0 gram) shows pictures of early scurvy as in No. 127.

Diagnosis: Scorbut mitior latens extensus. Colitis ac.

No. 129. Light brown—white—black.

Dead and autopsied $^{21}/_{4}$: Hair not loosening. No hemorrhage. Teeth firm? Upper jaw not brittle. Somewhat increased fragility of epiphyses, not of diaphyses; knees and costochondral junction slightly swollen. »White line» in the latter. Lively hyperemia of the mucous membrane of larynx, trachea, ventricle and duodenum. Liver 23.1 grams, spleen 1.0 gram. Histological exmination similar to that in No. 127.

Diagnosis: Scorbut latens extensus. Laryngo-tracheitis ac. Gastro-duodenitis ac.



×× *tubercular animals.*

Fig. 120. Series XXVIII. 0.2 m. pr. d.

No. 130. Yellow—black—white.

Progress to death $^{29}/_{4}$, findings at the *post-mortem* examination $^{30}/_{4}$ and histological examination similar to those in No. 129. Spleen 1.8 gram. Tooth, Fig. 23.

Diagnosis: Scorbut mitior latens extensus. Infectio.

No. 131. White—black—brown.

Dead $^{19}/_{4}$, autopsied $^{21}/_{4}$. Rather fat animal. Hair easily loosening. Knees swollen in the epiphyseal lines. Hemorrhages around several ribs. The costochondral junctions swollen, surrounded by pale grey enlargements (connective tissue). The teeth are removed with some difficulty from their alveoli. Liver 18.9 grams. Spleen 1.5 gram. Hyperemia of the upper part of the large intestine. Histological examination similar to No. 127.

Diagnosis: Scorbut mitior manifestus. Colitis ac.

No. 132.

♂. Brown—grey—white.

Dead and autopsied $^{11}/_{5}$: Hair easily loosening. Teeth somewhat loose, can not be lifted out. The costochondral junctions and knees somewhat

swollen. The epiphyses of the long bones brittle, diaphyses and upper jaw not. No hemorrhages. The primary tuberculous focus in the musculature of the right thigh consists of an almond-sized caseous mass, bordered by a capsule thin as a knife-edge. Lmphgl. genu et inguen. dx., lumbal., for the greater part occupied by caseous foci. Other lymph-glands slightly enlarged uniformly. Liver mottled, 18.5 grams. Spleen 1.4 gram. Histological examination of all ribs and of knees shows pronounced scurvy changes, *i. a.*, calcified necroses in the muscles. For the rest the same organs as in No. 104 are examined. Heart, Fig. 70. Heart and lungs also stained with cresylic violet, spleen on amyloid.

Diagnosis: Scorbut mitior manifestus. Tbc prim. loc., lmphgl. region.; lienis; hepatis; lmphgl. divers.; costar. duo.

No. 133.

♀. White—brown—black.

Dead and autopsied $^{23}/_{6}$. Hair easily loosening. The molars somewhat loose. The upper incisors easily broken. The costochondral junctions show white line, somewhat swollen, as are also the knees. Fracture of left ankle, healed in a wrong position, with slight, soft callus. Increased fragility of the epiphyses of the long bones. Upper jaw brittle. No hemorrhage except in spleen, 20.1 grams, and liver 39.8 grams, which show a very mottled picture. Local focus smaller than a hazel-nut, caseously changed, surrounded by a thin capsule, which is glossily reflecting. Lymph-glands of right knee and groin pea-sized, caseously changed. The lumbar glands bean-sized, homogeneously grey, as are also the bronchioles. Histological examination as in No. 132, and besides of kidney, adrenal, lung.

Diagnosis: Scorbut mitior manifestus. Tbc prim. loc., lmphgl. region., lienis, hepatis, lmphgl. divers.

No. 134. Black—brown—white.

No sign of scurvy. The stitch in the musculature of the right thigh without reaction. Abdominal cavity filled by a turbid liquid, which is scentless and contains numerous fat-drops and tissue-fragments. In the place of the pancreas there are only seen some small strips of tissue left. Right lung pneumonic. Histological examination of spleen, liver, lung.

Diagnosis: Pneumonia ac. dx. Necrosis ac. pancreat. c. peritonit.

Conclusion for Series XXVIII: The two tubercularly infected animals that had lived more than a month, show a certain connective-tissue reaction, in the shape of a thin capsule around foci in muscles and regional lymph-glands.

Series XXIX.

Animals 135—142. Of these No. 139—142 were infected with tubercle bacilli. All had basal diet and besides 1 ccm. of the earlier described preserved orange juice (0.3 m. pr. d.). Weight charts, Fig. 121.

No. 135. Black—white.

Dead $^{19}/_{8}$ without having shown scurvy symptoms. Autopsied the same day: Incisors not glossy, break easily. Teeth firm. Upper jaw brittle. Bones for the rest firm. Joints not swollen. No hemorrhage. In the abdominal cavity a couple of tea-spoonfuls of bloody liquid. Spleen 2.5 × 2.5 × 4 cm., weight 13.4 grams, very much filled with blood and fragile. The upper pole adherent to the back abdominal wall, bounding an abscess which is outwardly bounded by the 11th and 12th ribs. An irregular rupture through the spleen, big as the tip of a little finger leads into this abscess. Liver 44.5 grams, large,

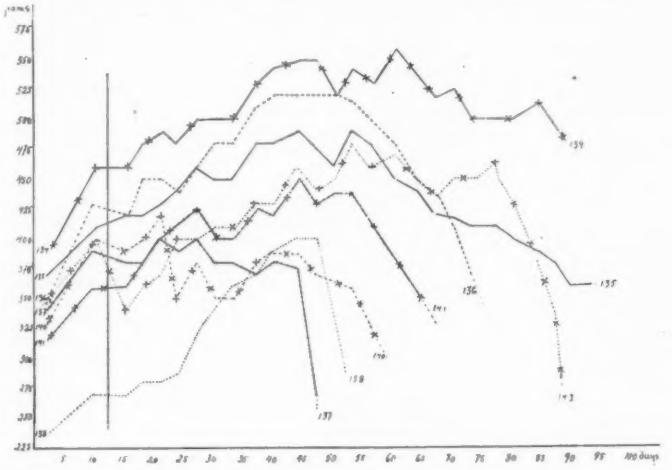
with swelling, muddy section surface. Histological examination as in No. 5, and besides of kidney. Tooth, Fig. 24.

Diagnosis: Scorbut mitior latens extensus. Abscessus lienis rupturat.

No. 136. Black—white—brown.

Dead $^{1}/_{8}$, autopsied $^{3}/_{8}$. Progress, findings and histological examination (also adrenal) similar to those in No. 135. Teeth in lower jaw somewhat loose. The costochondral junction somewhat swollen, the knees not. Spleen 3.5 grams, liver 33.5 grams. Abscesses in spleen and liver, partly into the substance, partly outwardly bounded by abdominal wall and kidneys. No rupture of these abscesses.

Diagnosis: Scorbut mitior latens extensus. Abscessus lienis et hepatis.



×× *tubercular animals.*

Fig. 121. Series XXIX. 0.3 m. pr. d.

No. 137. Brown—black—white.

Dead $^{5}/_{8}$, autopsied $^{6}/_{8}$. Coat rough, thin. Hair coming off in tufts. The diaphyses of the long bones are of an increased fragility. Teeth firm. Lymph-glands at the angle of the jaws bean-sized. Spleen 0.45 gram, liver 16.9 grams. Histological examination of organs as in No. 5 gives pictures similar to those in No. 135.

Diagnosis: Scorbut mitior latens extensus. Infectio.

No. 138. Black—white—brown.

Dead $^{8}/_{8}$, autopsied $^{9}/_{8}$. Hair coming off in tufts. No hemorrhage. Teeth firm. Upper jaw brittle. The epiphyses of the long bones brittle. Larynx filled with glassy phlegm. Liver 26.6 grams, spleen 1.7 gram. Histological examination as in No. 135. Spleen, Fig. 85, also stained on amyloid, iron, with Giemsa.

Diagnosis: Scorbut mitior latens extensus. Laryngitis ac.

No. 139.

♀. Grey—white.

Dead and autopsied $^{14}/_{8}$. Fat animal. Hair easily loosening. No hemorrhages except in the subcutis of right thigh, which is edematous. Walnut-sized, caseous focus in the musculature, surrounded by a connective-tissue capsula, 1 mm. thick. Lymph-gland of right knee not macroscopically changed. In the right groin two pea-sized, yellowish white glands, one of them caseous. Lymph-glands for the rest homogeneously swollen. Teeth firm, except incisors, which are rather loose and brittle. Upper jaw brittle. The epiphyses show increased fragility, the diaphyses not. The costochondral junctions somewhat swollen, distinctly in C 2 dx. and C 3 sin., there an enclosing connective-tissue formation is seen. Knees and other joints not swollen. Liver and spleen considerably enlarged; liver grey-yellow, adipose, fairly firm, 44.2 grams; spleen 2 × 4 × 6 ccm., 15.2 grams, profusely filled with blood, penetrated by white, firmer foci, big as a pin's head and more. In its upper pole a rupture, reaching almost across the organ. In the abdomen some tea-spoonfuls of bloody liquid. Histological examination as in No. 136. Rib, Fig. 38, also stained on iron and on fibrin according to Weigert.

Diagnosis: Scorbut mitior latens extensus. Tbc prim. musc., lmphgl. region., lienis, hepatis, lmphgl. divers. Hemorrhagia e ruptura lienis.

No. 140. All white (albino).

Dead $^{14}/_{8}$, autopsied $^{16}/_{8}$. Hair somewhat loose. No hemorrhage. Teeth somewhat loose, incisors chalky. Slightly increased fragility of epiphyses, but not of diaphyses. Upper jaw brittle. In the costochondral junctions the white line of Fraenkel. In the adductors of right thigh a bean-sized dry caseous focus, with a thin but distinct membrane-like capsule. The inguinal lymph-glands lentil-sized, white, hard as calcium, grate against the knife. Other lymph-glands homogeneously swollen. Liver 26.5 grams. Spleen 21.2 grams, profusely filled with blood, with large white soft portions of irregular form. Histological examination as in No. 104. Rib, Fig. 35. Spleen also stained on amyloid.

Diagnosis: Scorbut mitior latens extensus. Tbc prim. musc., lmphgl. region., lienis, hepatis, lmphgl. divers.

No. 141. Brown—white.

Dead $^{22}/_{8}$, autopsied $^{24}/_{8}$. Teeth somewhat loose, brittle. Upper jaw rather brittle. Pairs of ribs 3—5 have enlarged costochondral junctions. Knees slightly swollen in the epiphyseal regions. Hemorrhage in subcutis around the left elbow. From the inside of right knee the subcutis, upwards over the abdomen and forwards against both axillæ, is changed into caseous tissue, a couple of mms. thick. The pelvic lymph-glands are bean-sized and occupied to about half their volume by caseously purulent foci. Spleen 2.2 grams, liver 27.5 grams. Histological examinations as in No. 105.

Diagnosis: Scorbut mitior latens extensus. Tbc subcutis, lmphgl. region., lienis, hepatis.

No. 142.

♂. Brown—black—white.

Dead and autopsied $^{13}/_{8}$: lean animal. Teeth firm. Incisors very brittle. No hemorrhage. No swelling of the epiphyses of the extremities, nor of the costochondral junctions. Epiphyses easily broken, diaphyses not. Primary focus in the thigh musculature big as a brown bean, with thin, translucent capsule. Of some rice-shaped inguinal glands, one shows a small caseous focus, another a similar focus which is partially calcified and surrounded by a distinct connective-tissue capsule. Other lymph-glands homogeneously

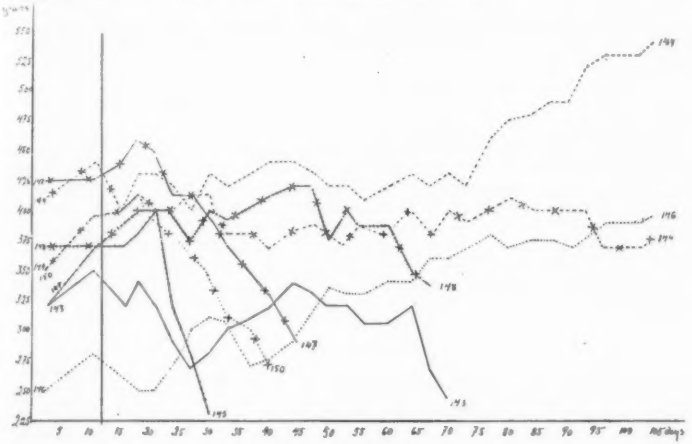
glassily swollen. Larynx reddened. Mucous membrane wrinkled and swollen, on its surface a slight quantity of phlegmy, turbid, bubbly fluid. Mucous membrane in trachea reddened. Liver 19.6 grams. Spleen 2.4 grams. Histological examination as in No. 105, and besides of heart, lung. Kidney, Fig. 88.

Diagnosis: Scorbut mitior latens extensus. Tbc prim. musc., lymphgl. region. et aliar., lienis, hepatis. Laryngo-tracheit. ac.

Conclusion for Series XXIX: Distinct, but slight connective-tissue reaction around tuberculous foci.

Series XXX.

Animals 143—150. Of them No. 147—150 were infected with tuberculosis. All the animals had basal diet and with that each 1.5 ccm. of preserved orange juice (0.5 m. pr. d.). Weight charts, Fig. 122.



×× *tubercular animals.*

Fig. 122. Series XXX. 0.5 m. pr. d.

No. 143. White—black—brown.

Dead $^{26}/_{5}$, autopsied $^{30}/_{5}$: very lean. No macroscopical sign of scurvy. Liver (11 grams) shows, like spleen (0.3 gram), lung, lymph-gland above the right adrenal, foci of irregular form and varying sizes up to the size of a bean, peripherally hard, in the centre often purulent, of white-yellow colour. Histological examination shows them to consist of a non-specific granulation tissue. Scorbutic changes in 13 ribs, spleen

Diagnosis: Scorbut latens extensus. Infectio.

No. 144.

♂. Brown—grey—white.

Chloroformed and autopsied $^{29}/_{6}$. No macroscopical sign of scurvy or infection. Liver 29.2 grams. Spleen 1.9 gram. At the histological examination of 11 ribs, normal junction pictures are shown. Teeth, Fig. 25. Spleen also stained with Giemsa, heart, kidney, adrenal, muscle.

Diagnosis: Scorbut mitior latens levior.

No. 145. Grey—white—black.

Dead and autopsied $^{13}/_{4}$. Incisors of lower jaw chalky, somewhat loose. For the rest, no sign that might indicate scurvy. Liver 18.8 grams. Spleen 0.8 gram. The right foot shows pathological changes. The claw-bed is injected, the claws partly gone. The lymph-glands at the knees to some degree swollen. Injection of their arteries. The lungs have diminished air contents. The bronchi show purulent contents. Histological examination as in No. 97, and besides of heart (Fig. 68, 69) and right paw. Heart and lung also stained with cresylic violet.

Diagnosis: Scorbut mitior latens levior. Gangrena extremitat. Bronchitis purulenta.

No. 146.

♂. White—black—brown.

Chloroformed and autopsied $^{29}/_{6}$ 1923. Incisors of the lower jaw possibly not quite firm. For the rest no pathological symptoms. Histological examination as in No. 97.

Diagnosis: Scorbut mitior latens levior.

No. 147. Black—white.

Dead and autopsied $^{30}/_{4}$: no macroscopical sign of scurvy or acute infection. The right inguinal lymph-gland pea-sized, some partially changed into a dry caseous mass, others fibrous. Submaxillary lymph-glands pale, homogeneously swollen. Liver 24.8 grams with numerous foci, partly caseating but otherwise hard, up to the size of beans. Spleen 2.1 grams. The large intestine in two places adherent through the mesentery round a caseous lymph-gland. Histological examination as in No. 104, and besides of colon.

Diagnosi:: Scorbut latens levior. Tbc prim. musc., lmphgl. region., lienis, hepatis, pulmon., coli; lmphgl. divers.

No. 148. Black—brown—white.

Dead and autopsied $^{24}/_{5}$. Upper jaw brittle. Diaphyses somewhat easily broken. Epiphyses not. No sign of scurvy. The caseated, a little more than hazelnut-sized primary focus does not lie in the musculature but subcutaneously, surrounded by a very thin, reflecting membrane. Lymph-glands at the right knee and in the inguen pea-sized and a little larger, with small caseous foci, otherwise rather hard. Small quantity of turbid liquid in abdominal cavity and left pleura. Lower part of the lower lobe of left lung pneumonic. Peritoneum parietale rose-coloured, downy, with fibrin films on left lobe of the liver and on spleen. Liver 21.5 grams. Spleen 1.2 gram. Histological examination as in No. 116.

Diagnosis: Scorbut mitior latens extensus. Tbc prim. musc., lmphgl. region., lienis, hepatis, lmphgl. divers. Bronchopneumonia ac. c. pleurit. et peritonit. ac.

No. 149.

♂. Grey—brown.

Chloroformed and autopsied $^{29}/_{6}$. No macroscopical sign of scurvy or acute infection. The primary focus in the thigh musculature bean-sized, caseating though not yet homogeneous, outwardly bordered by a homogeneous granulating muscle surface. Lymph-glands everywhere homogeneously swollen. without distinct foci. Spleen 11.2 grams. In the lower pole a pea-sized whitish yellow focus. Liver 43.8 grams, traversed by strands of what looks like connective-tissue. Lungs filled with a large number of small foci, miliary in trefoil

or horseshoe arrangement. Histological examination as in No. 116. Spleen also stained on amyloid.

Diagnosis: Scorbut mitior latens extensus. Tbc prim. musc., lmphgl. region., lienis, hepatis, pulmon., lmphgl. divers.

No. 150. Grey—yellow.

Dead $^{26}/_{4}$, autopsied $^{17}/_{5}$: No macroscopic sign of scurvy. In the bend of the right knee between the tendons of the adductors, a great focus of fibrous tissue. Lymph-glands at knees, groins and in pelvis caseating, not purulent, hardly more than pea-sized, enclosed by a capsule, from which they are easily loosened. In the mesentery some pea-sized hard lymph-glands. Spleen 0.8 gram, liver 11.8 grams. Histological examination as in No. 117.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region. lienis, hepatis, pulm., lmphgl. divers.

Conclusion for Series XXX: The reaction of the connective-tissue stronger than in preceding series, but not of normal strength.

Series XXXI.

Animals 151—158. Of these No. 155—158 were infected with tuberculosis. All animals had together with the basal diet 2 ccm. of preserved orange juice (0.7 m. pr. d.). Weight charts, Fig. 123.

No. 151.

♂. White—brown.

Killed and autopsied $^{29}/_{5}$. No macroscopical sign of scurvy or acute infection. Rather fat animal. Liver 29.9 grams. Spleen 1.1 gram. Histological examination as in No. 5.

Diagnosis: Scorbut mitior latens levior.

No. 152. Grey—white.

Dead $^{20}/_{4}$, autopsied $^{21}/_{4}$. The long bones generally brittle (diaphyses). No sign of scurvy. In lungs, liver, right kidney, different muscles and two ribs, there are foci up to the size of a hazel-nut, yellow, which at incision are found to contain a creamy mass in the centre. Histological examination as in No. 5. Tooth, Fig. 26.

Diagnosis: Scorbut mitior latens levior. Infectio.

No. 153.

♀. Black—brown—white.

Died and was autopsied $^{27}/_{5}$. Rather fat animal. Upper jaw brittle. Incisors of lower jaw somewhat loose. Otherwise no sign of scurvy. In both uterine horns lively injection around an elevated area 5—6 mm. long, on the inside showing a cavity with a small irregular elevation (graviditas). Mucous membrane in larynx, trachea and bronchi reddened. All left lung pneumonic, over a large extent fastened through light red adherences to pleura parietalis. Between the adherences abundant bloody-serous liquid. Liver 23.2 grams, spleen 1.2 gram. Histological examination as in No. 5.

Diagnosis: Scorbut mitior latens levior.

No. 154. Yellow—black—white.

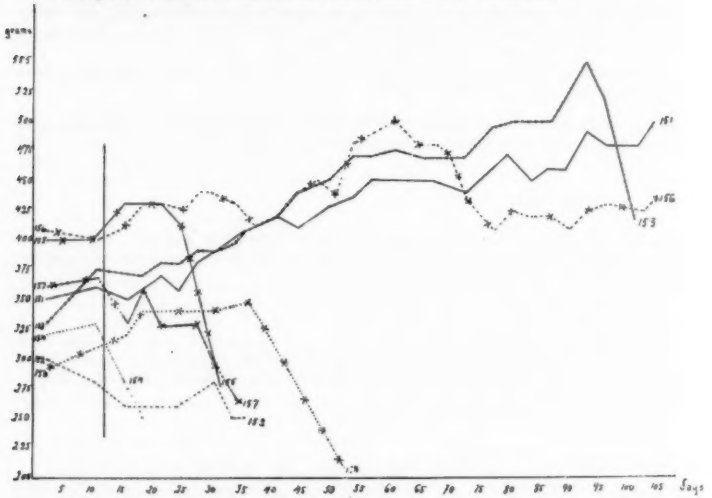
Dead $^{4}/_{5}$, autopsied $^{5}/_{5}$. Nowhere any pathological conditions. Microscopical examination not undertaken.

Diagnosis incerta.

No. 155. White—black—brown.

No macroscopical sign of scurvy. Strong injection of duodenum, in the descending part of which there is a small callous ulcus. Towards the intestine there are two lymph-glands attached together, large as the half of an almond. In one of them a large abscess with thin pus. Liver 22.5 grams. Spleen 1 gram. Histological examination as in No. 104. In the thigh musculature only degeneration and increased connective-tissue are found, but no necrosis, no specific granulation tissue, no tubercle bacilli.

Diagnosis: Scorbut mitior latens levior. Ulcus duodeni.



×× *tubercular animals.*

Fig. 123. Series XXXI. 0.7 m. pr. d.

No. 156.

♂. White—black.

Chloroformed and autopsied $^{29}/_{6}$. Rather fat animal. Macroscopically no sign of scurvy. In the adductors of the right thigh two pea-sized foci with a connective-tissue capsule, a little above 1 mm. thick. Knee lymph-glands on both sides bean-sized, with small caseous foci, surrounded by a calcium-grating capsule. Calcified, partially liquified foci are also found in several submaxillary lymph-glands. In lung hilus small hard lymph-glands without distinct calcium scrapings. Numerous miliary, not quite round grey-white foci in lungs and liver (38.4 grams) some few in spleen (4.8 grams). A bean-sized focus, calcified and caseating, is seen at the back in the middle part of the liver. Histological examination as in No. 104. Tooth, Fig. 27.

Diagnosis: Scorbut mitior latens extensus. Tbc prim. musc., lmphgl. regional. et divers.; lienis, hepatis, pulmon.

No. 157. Brown—white—black.

Died $^{20}/_{4}$, autopsied $^{23}/_{4}$. Teeth somewhat loose. Upper jaw not brittle. Costrochondral junctions and knees slightly swollen. Hemorrhage around

right knee-joints. Increased fragility of the epiphyses of the long bones. Spleen 0.4 gram. Liver 12 grams. Local focus in the musculature of right thigh has the shape of an elongated narrow abscess, without capsule. Lymph-glands in groin and in pelvis somewhat enlarged, without foci. A piece of the small intestine, a few cm. long, shows lively hyperemia with blood-imbibed faeces. Histological examination as in No. 116. The epiphyses of knees and elbows show no certain scorbutic changes.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region. Enteritis hemorrhagica.

No. 158.

♀. Black—brown—white.

Died $^{8}/_{5}$ and was autopsied $^{9}/_{5}$. No macroscopical sign of scurvy. On the right side of the nose a region which is partly hairless, partly covered by short, broken hairs. In the base of the plantar side of the little toe on the right hind-leg a small hyperemic blain. In the nostril milky liquid. Trachea filled with frothy liquid, a little thinner than milk. In the muscles of the right thigh several pea-sized abscesses, enclosed by connective-tissue capsules. Regional glands pea-sized, at the most, with miliary foci of caseous tissue in one pole. Lung hilus glands similar, but fibrous. Spleen 6.3 grams. Liver 17.3 grams. Histological examination as in No. 116. Spleen also stained on amyloid.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region., lienis, hepatis, pulmon.

Conclusion for Series XXXI: The strength of the connective-tissue reaction varies in the different cases — from fairly strong to rather weak.

Series XXXII.

Animals 159—166. Of these No. 163—166 were infected with tubercle bacilli. The animals had basal diet and in addition each 2.5 ccm. (0.8 m. pr. d.) of preserved orange juice. Weight charts, Fig. 124.

No. 159. Black—white.

Dead and autopsied $^{27}/_{4}$. No macroscopic sign of scurvy. A deep reddening of the mucous membrane in the digestory canal from stomach to anus, increasing downwards. In the mesentery of the large intestine a purulent lymph-gland. Liver 19.5 grams. Spleen 0.5 gram. Histological examination of 12 ribs, spleen and liver. Tooth Fig. 28.

Diagnosis: Scorbut mitior latens levior. Gastro-enterocolitis ac. c. lymphadenit. supp.

No. 160.

♀. White—black—brown.

Chloroformed and autopsied $^{29}/_{4}$. Fat animal. Hair somewhat loose. No sign of scurvy or acute infection. Liver 31.2 grams. Spleen 1.3 gram. Histological examination of 12 ribs, muscles, jaw, liver, spleen; heart and lungs, also stained with cresylic violet.

Diagnosis: Scorbut mitior latens levior.

No. 161.

♀. Black—white—brown.

Chloroformed and autopsied $^{29}/_{4}$. Hair somewhat loose. No macroscopical sign of scurvy or acute infection. Liver 31.5 grams, spleen 1.5 gram. Histological examination as in No. 160 (spleen also stained according to Giemsa, tooth, Fig. 29, and besides of heart, Fig. 66, kidney, Fig. 89, adrenal.

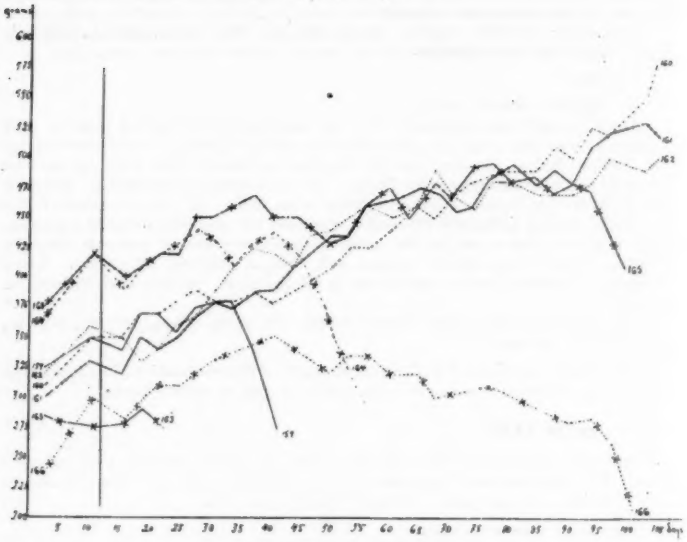
Diagnosis: Scorbut mitior latens levior.

No. 162.

♀. Grey—brown—white.

Progress, macroscopical and microscopical examinations and findings as in No. 161. Liver 28.5 grams, spleen 1.5 gram.

Diagnosis: Scorbut mitior latens levior.



×× *tubercular animals.*

Fig. 124. Series XXXII. 0.8 m. pr. d.

No. 163. Grey.

Died $^{9}/_{4}$, autopsied $^{10}/_{4}$. No macroscopical sign of scurvy or tuberculosis. On the front side of the lower part of sternum an enlargement of the periosteum, 1 × 1 cm., homogeneous, grey, soft, with an abscess in the centre. In the left pleura and in the pericardium some ccm. of bloodily turbid liquid. On visceral pleura and pericardium thin fibrinous membranes. Left lung filled with miliary, greyish white nodules. Cor nearly ballshaped. In the left auricle a thrombus, which fills the whole space and is adherent to the wall. Histological examination of the mentioned organs, 24 ribs, knees, spleen, liver, teeth, thigh focus and lymph-glands.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region., lienis, lmphgl. hil. pulm. Pneumoniæ, pleuritis, pancarditis. Periostit. sternal.

No. 164. Black—white.

Died $^{12}/_{4}$, autopsied $^{13}/_{4}$. In the larynx glassy phlegm and a small quantity of a thin turbid liquid. Mucous membrane in trachea and bronchi reddened. Lungs have diminished air content. No sign of scurvy. In thigh musculature

on the right side scattered caseous foci, peasized, with distinct, though thin, connective-tissue capsule. In lympho-gland. genu et inguen. dx. and in the regional pelvic glands, which all are smaller than a pea, there is found in one pole miliary foci, one in each, looking like yellow cheese, but under the knife like hard cicatrized fibrous tissue. Liver 23.7 grams, mottled. Spleen 0.6 × 1.3 × 3.7 cm., weight 3.5 grams, of similar, mottled appearance. Histological examination as in No. 116.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region., lienis, hepatis, pulmon., lmphgl. divers., costar. duo, condyl. femoris. Laryngo-tracheo-bronchitis and bronchopneumonia ac.

No. 165.

♀. Black—brown—white.

Died and was autopsied $^{27}/_{8}$: Hair loosening. The epiphyses of the long bones somewhat more easily broken than normally, diaphyses not. For the rest no sign of scurvy. Right lung to pleura parietalis with soft, red adherences. Lungs filled with foci in sizes from a pin's head to a pea, greyish white in the periphery, yellow white in the centre, not purulent. In superficial parts towards pleura a number of conical foci. Spleen 11.5 grams, large, mottled, filled with a large number of calcium-hard foci, big as a pin-point. Liver 68.0 grams, paler, granulated, like spleen very firm with hard pale regions up to the size of a hazel-nut, in which there are caseous foci. In lymph-glands of right knee and groin, and in the regional pelvic glands, all of them at the most pea-sized, fibrous, very hard foci with small, miliary, caseous abscesses in the centre. In some of them the caseous focus is not a uniform cavity but is divided by connective-tissue septa into different rooms. Glands of lung hilus similar, a little larger, but without abscesses. Instead the focus is felt to be calcium-hard. Histological examination as in No. 116, except of adrenal.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region. lienis, hepatis, pulmon., lmphgl. divers.

No. 166. White—yellow.

Showed from the start a bad appetite. A couple of weeks after the weight curve had turned downwards, the animal began persistingly to twist its head and wheel round to the right. Showed this symptom afterwards, only the twisting was during the last week to the left, till death $^{26}/_{8}$. Autopsied $^{27}/_{8}$. General brittleness of bone. Extreme emaciation. No sign of scurvy. The terminations of all the four extremities mutilated, the tips of the toes being gone on the fore-paws, the distal part of the foot as far as half the metatarsus on the hind-paws. Remaining stumps dry, brittle, easily broken. Lymph-glands in axilla and inguen strongly hyperemic. Cultures are made on the juice from these glands on aërobical and anaërobical substrata; no growth. In the thigh musculature on the right side a small necrotic focus, enclosed by a distinct capsule. In the right knee, groin and regional pelvic glands small whitish yellow foci. In the centres of these there is a minimal abscess in one pelvic lymph-gland as well as in one lung hilus gland. Spleen 2.8 grams, liver 18.8 grams. In the lower part of right lung a couple of small miliary, gelatinous granulations. Histological examination of the mentioned organs and of 10 ribs, muscles, jaw.

Diagnosis: Scorbut mitior latens levior. Tbc prim. musc., lmphgl. region., lienis, hepatis, pulmon., lmphgl. divers. Gangrena extremitat.

Conclusion for Series XXXII: Connective-tissue reaction of moderate strength round tuberculous foci.

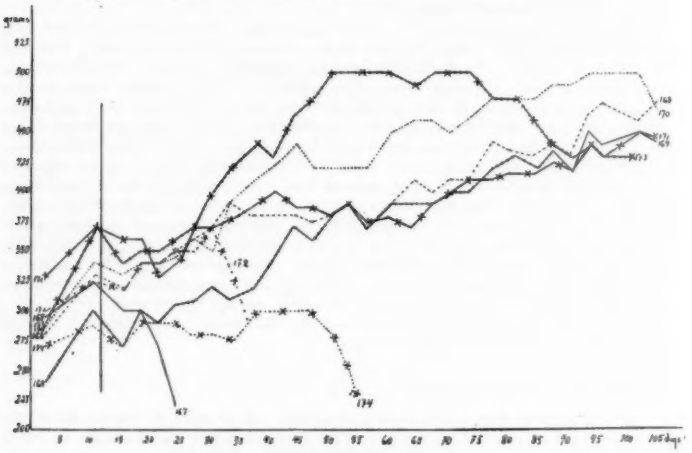
Series XXXIII.

Animals 167—174. Of these No. 171—174 were infected with tubercle bacilli. All animals had from March 29 basal diet and besides each 3.5 ccm. of preserved orange juice. They were completely protected. Weight charts, Fig. 125.

No. 167. Whitish grey.

Died $^{10}/_{4}$, autopsied $^{13}/_{4}$. No sign of scurvy. Strong hyperemia of colon. Lymph-glands in the mesentery enlarged. Spleen 0.1 gram. Liver 17.7 grams. The eighth rib on the right shows in the costochondral junction a heavy local enlargement. Histological examination of 2 ribs, jaw, liver, spleen.

Diagnosis: No scurvy. Colitis ac. Osteochondrit. ac.



×× *tubercular animals.*

Fig. 125. Series XXXIII. 1.2 m. pr. d.

No. 168.

♀. White—black—brown.

Killed and autopsied $^{30}/_{4}$. No pathological conditions could be observed. Histological examination of teeth, liver (29.2 grams), spleen (1.0 gram), kidney, Fig. 86; heart, also stained with cresylic violet.

Diagnosis: No scurvy.

No. 169.

♀. Brown—black—white.

Progress and findings as in No. 168. Liver 13.3 grams, spleen 0.8 gram.

Diagnosis: No scurvy.

No. 170.

♀. Brown—black—white.

Progress and findings as in No. 168. Liver 23.1 grams, spleen 0.9 gram.

Diagnosis: No scurvy.

No. 171.

♀. All white (albino).

Killed and autopsied $^{30}/_{5}$. Fat animal. No sign of scurvy. No macroscopical sign of tuberculosis. Liver 20.0 grams. Spleen 1.0 gram. At histological examination of the thigh musculature in series of sections, a submiliary focus was found, consisting of epitheloid cells, lymphocytes and fibroblasts. No tubercle bacilli found in it. Nothing remarkable noted in liver, spleen, jaw. Heart and lungs also stained with cresylic violet.

Diagnosis: No scurvy. Tbc prim. musc. peracta.

No. 172. White—brown—black.

Dead $^{22}/_{4}$, autopsied $^{23}/_{4}$. Fat animal. Hair not coming off. No sign of scurvy. Primary focus in thigh musculature rather more than pea-sized, hard-rinded with a miliary abscess in the centre. In the regional lymph-glands, which are pea-sized, there are miliary, yellow, very hard foci. Spleen weighs more than 1 gram. Right lung in its upper part pneumonic, adherent to pleura parietale. In the pleura bloody liquid. Histological examination as in No. 165, and besides of jaw. Region. lymph-gland, Plate V.

Diagnosis: No scurvy. Tbc prim. musc., lmphgl. region., lienis, hepatis. Pneumonia ac. dx.

No. 173. White—black.

Fat animal. Hair not loosening. No sign of scurvy. Teeth firm. Incisors of lower jaw brittle, easily broken. In the musculature of the right thigh a more than almond-sized, caseous focus with a smooth capsule more than a millimeter thick. One lymph-gland in knee and one in groin, pea-sized with a miliary abscess, enclosed by rind-like connective-tissue. Other lymph-glands homogeneously swollen. Abdomen distended. In the abdominal cavity a tea-spoonful of liquid blood. The large intestine considerably distended by gases. A rupture a centimeter long in the lower pole of the spleen, which is swollen, congested, around a pea-sized greyish yellow focus. Under slight pressure blood percolates from the rupture. Spleen 10.2 grams. Liver 35.5 grams. Histological examination of jaw, thigh focus, different lymph-glands, liver, spleen.

Diagnosis: No scurvy. Tbc prim. musc., lmphgl. region., lienis, hepatis, lmphgl. divers. Ruptura lienis c. peritonitide.

No. 174.

♀. Brown—black—white.

Died and was autopsied $^{11}/_{5}$. No sign of scurvy. Between the tendons of the adductors in the bend of the right knee an almond-sized caseous focus, surrounded by connective-tissue rinds, a millimeter thick. Gland in the bend of knee pea-sized, white, hard. Other lymph-glands homogeneously swollen. Spleen 0.9 gram. A somewhat more than pea-sized splenculus at the spleen hilus, largely caseous. Liver 18.0 grams, mottled, with differently sized, irregular white foci. Histological examination as in No. 172.

Diagnosis: No scurvy. Tbc prim. musc., lmphgl. region., lienis, hepatis, lmphgl. divers, costar. duo.

Conclusion for Series XXXIII: Strong reaction of a well developed connective-tissue in and about tuberculous foci.

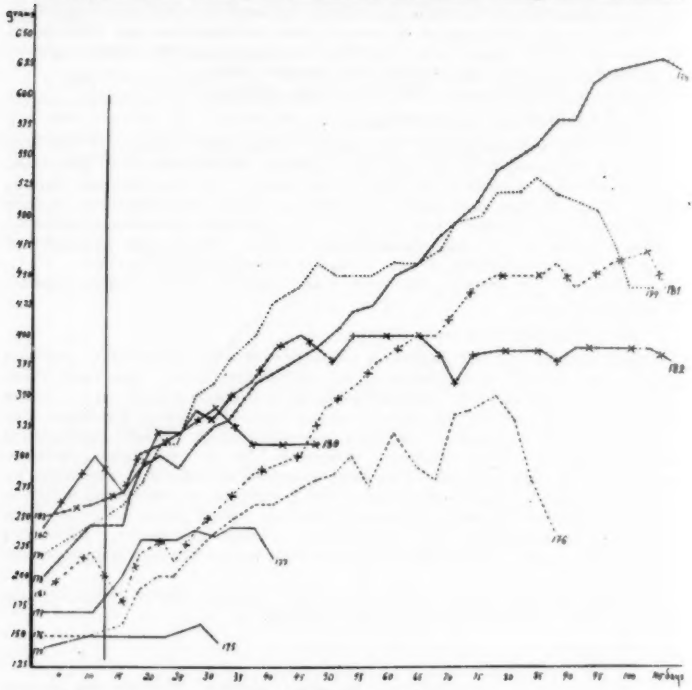
Series XXXIV.

Animals 175—182. Of these No. 180—182 were infected with tubercle bacilli. All the animals had basal diet and besides 5 ccm. of preserved orange juice. The dose proved to be fully protective. Weight charts, Fig. 126.

No. 175. White—black—brown.

No sign of scurvy. All claws partially gone. A metatarsal joint opened. Upper lobes of both lungs pneumonic. Histological examination as in No. 172.

Diagnosis: No scurvy. Pneumonia ac. bilat. Gangrena extremitat.



×× *tubercular animals.*

Fig. 126. Series XXXIV. 1.7 m. pr. d.

No. 176. Brown—white—black.

Died and was autopsied $^{13}/_{3}$. No sign of scurvy. The epiphyses of the long bones are more easily broken than normally. Upper incisors somewhat loose. The right pleura is reduced to slits between thick fibrin coats, through which the pneumonic lower part of the lung adheres to chest wall and diaphragm. In the peritoneal cavity a moderate quantity of frothy, turbid scentless liquid. Peritoneum rose-coloured. Liver 15.5 grams, spleen 0.8 gram. Histological examination as in No. 172. Tooth, Fig. 30.

Diagnosis: No scurvy. Pleuropneumonia ac. dx. et peritonitis ac.

No. 177. Brown—white.

Died $^{26}/_{4}$, autopsied $^{27}/_{4}$. No sign of scurvy. Mucous membrane in larynx wrinkled. Under the left mandible a pea-sized, half purulent lymph-

gland. In both lungs miliary pneumonic foci. Liver 12.4 grams, spleen 0.5 gram. Histological examination of spleen, liver, jaw.

Diagnosis: No scurvy. Laryngotracheit. ac. Bronchopneumoniæ ac.

No. 178.

♂. Black—brown—white.

Chloroformed and autopsied $^{30}/_{6}$. Fat animal without remark. Liver 39.9 grams. Spleen 1.0 gram. Histological examination of spleen, liver, jaw, kidney. Adrenal, Fig. 92.

Diagnosis: No scurvy.

No. 179.

♂. Greyish yellow.

Chloroformed and autopsied $^{30}/_{6}$. No sign of scurvy. Hair loosening rather easily. Upper lobe of right lung pneumonic. Lymph-glands in hilus homogeneously swollen. Liver 25.6 grams, spleen 0.7 gram. Histological examination of liver, spleen, jaw.

Diagnosis: No scurvy. Pneumonia ac.

No. 180. Grey—brown—white.

Dead and autopsied $^{6}/_{8}$. No signs of scurvy. In the musculature on the inside of the right thigh very strong rind formation with a number of small caseous miliary foci. Lymph-glands in the right groin and in pelvis pea-sized, hard, with miliary, strongly white foci of great hardness, without cheese. Spleen (2.2 grams) shows a large number of larger and smaller soft parts of different red colour. Liver 21.6 grams, with a large number of conical whitish yellow parts localized at the border with hyperemia in the edges (septic infarcts). All the left lung and central parts of the two upper lobes in the right lung pneumonic, with turbid black fluid. Two Peyer's plaques hyperemic, swollen. Histological examination as in No. 104.

Diagnosis: No scurvy. Tbc prim. musc., lmphgl. region., lienis, hepatis. Bronchitis ac. Pneumonia ac.

No. 181.

♂. Black—yellow—white.

Dead and autopsied $^{30}/_{8}$. No sign of scurvy. In the right thigh musculature an irregular cavity reaching a good distance towards inguen, filled by a thin liquid with strips of tissue and bordered by thick rinds of connective tissue. Lymph-glands lying at right knee and groin, in left musculus quadriceps and at left knee, and in pelvis, pea-sized, with miliary and smaller caseous abscesses, enclosed by thick connective tissue. A similar gland under the jaw. In one of the pelvic glands a similar small focus with calcium in the capsule. Liver large, 37.9 grams, congested, with some miliary granulations, greyish white. Spleen 2.8 grams, likewise. Histological examination as in No. 104.

Diagnosis: No scurvy. Tbc prim. musc., lmphgl. region., lienis, hepatis, lmphgl. divers.

No. 182.

♂. Black—brown.

Killed and autopsied $^{30}/_{6}$. No sign of scurvy. Not much hair loosening. The diaphyses of the long bones and upper jaw somewhat more brittle than normally. In the adductors of the right thigh a narrow, less than almond-sized focus of dry cheese, bordered by a distinct capsule. In the left thigh, in the adductors, a lymph-gland, with an abscess in the centre, and in the outer parts changed into a thick connective-tissue membrane. Lymph-glands at both knees pea-sized, white, fibrous, no foci. Other lymph-glands generally

swollen, grey, homogeneous. Liver 44.8 grams, mottled, filled with submiliary, somewhat irregularly formed grey foci with hyperemic zone. Lungs likewise. Also in the spleen some similar foci. Histological examination as in No. 104.

Diagnosis: No scurvy. Tbc prim. musc., lymphgl. region.; lienis, hepatis, pulmon., lmphgl. divers.

Conclusion for Series XXXIV: Strong reaction of well developed connective tissue in and around tuberculous foci.

No. 183.

♂. Brown—white—black.

From the day of arrival, $^{19}/_{3}$ (weight 310 grams), the animal persistingly twisted its head to the left and would run round. It was put on complete dietary as Series 2. Standstill in weight till $^{19}/_{4}$, when increase in weight followed. In the middle of May the above-mentioned symptom disappeared and the animal seemed afterwards to be well. Chloroformed and autopsied $^{3}/_{7}$. Liver 33.0 grams. Spleen 0.6 gram.

Histological examination as in No. 5 shows normal pictures in most organs. Kidney, p. 99. The nerves in the bend of the knees show considerable changes: axis-cylinders irregularly swollen, myelinic sheath irregularly segmented; here and there small hyperchromatic, spool — starshaped cells with rounded nuclei.

Diagnosis: Beriberi (?) peracta.

Series XXXV.

Animals 184—187. These were put on relative general inanition with full dose of antiscorbutic from Oct. 1, 1923. Each animal had its own cage and got a daily ration of 40 grams of chickweed and besides a dose of preserved orange juice. This was given to each animal with a pipet in a dose of 3 ccm., and besides 10 ccm. were put into the cage, which were not always consumed. Weight charts, Fig. 127. The animals retained their liveliness of movement almost to the last day.

No. 184. Black—brown—white.

Dead and autopsied $^{9}/_{10}$. Hair not coming off. Almost no fat. No sign of scurvy. Bones not brittle, teeth firm. Liver 11.0 grams, spleen 0.2 gram. Histological examination of 12 ribs, jaw, muscles, heart, liver, lung, shows no changes like those described for the scorbutic animals. Kidney, adrenal, salivary gland, spleen, show slight atrophic changes of the parenchymatous cells.

Diagnosis: Inanitio.

No. 185. White—brown.

Died and was autopsied $^{14}/_{10}$. Lean animal. No sign of scurvy. Histological examination as in No. 184. Also liver (nuclei) and heart (elastic membranes) show slight atrophic changes. Hemorrhage in the marrow of the adrenal.

Diagnosis: Inanitio.

No. 186.

♀. White—brown.

Died and was autopsied $^{10}/_{11}$. Findings and histological examination as in No. 185. Adrenal, Fig. 94.

Diagnosis: Inanitio.

No. 187.

♀. White—brown.

Died and was autopsied $^{7}/_{10}$. Hair easily loosening. Lean animal. The diaphyses of the long bones are somewhat too easily broken. No sign of scurvy. Two lymph-glands in the lower jaw with miliary abscesses. Histological examination as in No. 184. Only kidney and adrenal show slight atrophic changes of the parenchymatous cells.

Diagnosis: Inanitio. Lymphadenit. ac. supp.

Conclusion for Series XXXV: With a dietary of about a third of that required for normal increase in weight, the animals lost in one to two weeks 29—36 % of their initial weight. The lymphoid tissue of the spleen, the elastic membranes of the large vessels, the parenchymata of kidney, adrenal and liver showed slight atrophic changes.

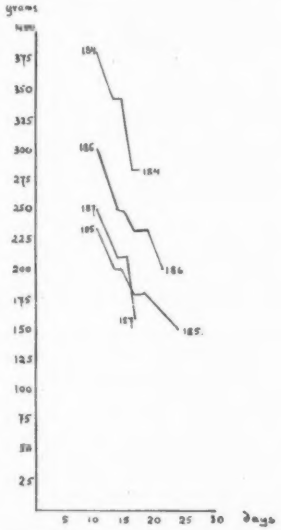


Fig. 127. Series XXXV. Relative inanititon.

Additional animals.

No. 188.

♂. Light brown—white.

Had from $^{1}/_{10}$ chickweed *ad lib.*, and was besides given 5 ccm. of preserved orange juice with pipet. Killed and autopsied $^{10}/_{10}$. Everywhere normal conditions, also at the histological examination as in No. 5. Tooth, Fig. 3.

Diagnosis: No scurvy.

No. 189. Black—brown.

From birth it has been fed on complete dietary by the breeder and seemed healthy when bought; weight 300 grams. Was killed immediately $^{1}/_{10}$ with chloroform and was autopsied. Examination as in No. 5 showed everywhere normal conditions. Radiograms of the ribs, Fig. 42 b.

Records belonging to Part IV, Chapter III.

Terms and abbreviations.

D 1, D 1—2, D 2, D 2—3, D 3, Dulness in five degrees.
Resp. respiration; *ves.* vesicular; *br.* bronchial.
R Râles.
Scl. fossa supraclavicularis; *I, II, III* etc. first, second, third etc. costal interstice; *ssp* fossa supraspinata; *sp.* spina; *A* angulus scapulae; *1/2 A* halfway between sp and A.
Pat. 2/13 patient second among thirteen children.
Expect. expectoration.
Infl. ep. influenza epidemica.

Couple a.

1. Or.

Ernst Bernhard L-n, born 1890. Farmer. Odensala.
Anamnesis. Pat. $^{1}/_{12}$. Two brothers died of tbc. Was well till 1916, when he had pleuritis exsud. bilat. Afterwards subjectively well till the autumn of 1922; then cough, expectoration, breathlessness. The physician suspected tbc pulm. in December 1922. No night-sweat; appetite fairly bad, during the last few months no emaciation. Never hemoptysis, never pneumonia.
Admitted $^{3}/_{2}$ 1923. *Status* $^{6}/_{2}$: Constitution fairly good. Spare flesh. Moderate cough with moderate amount of expect. Stitching and stabbing pain. Appetite fairly good. Digestion and sleep good. Feels well. Pulse: about 100. Temperature: sub-febrile till $^{29}/_{4}$, afterwards 38—39° C. Stomach, nose, pharynx, larynx 0.
Local status: D 3 over both lungs with bronchial respiration. Diffuse R over both lungs. In the lower left side lobe an orange-sized cavity, in the upper right side lobe a smaller cavity. Tbc of Stage III. all over the lungs.
Extracts from records. $^{2}/_{3}$ orange. $^{20}/_{3}$: R lessened in the bases. The rest as before. $^{1}/_{5}$: as before, yet the left side cavity increased anteriorly. $^{29}/_{5}$: since three weeks the patient has constant headache with vomiting. Babinsky +, Oppenheim +, stomach reflex 0, foot clonus, dull pupillar reflexes. Kernig +. During the last weeks temporarily wandering in mind, during last days periods of sopor. † $^{30}/_{5}$. Meningitis tbc.
Tbc bacilli always +. Examined every fortnight.
Summary: Tbc of Stage III. with cavities, which increase during the orange period (efter 6 weeks). After 2 months meningitis tbc. Cyanotic from the first; dissuaded from sanatorium treatment, being considered a hopeless case.

Weight chart:

$^{4}/_{2}$ — 69 kg.	$^{1}/_{3}$ — 71 kg.	$^{31}/_{3}$ — 71.5 kg.	$^{1}/_{5}$ — 69.5 kg.
$^{15}/_{2}$ — 71 »	$^{14}/_{3}$ — 71.5 »	$^{14}/_{4}$ — 69.5 »	$^{29}/_{5}$ — †

2.

Erik Fridolf A-n, born $^{25}/_{8}$ 1891. Building carpenter. Ed.
Anamnesis: Pat. $^{2}/_{3}$. A maternal aunt died of tbc. pulm. One of the patient's 3 children died of tbc. mening. Well till the autumn of 1918, then infl. ep. with pneum. sin. After that periods of coughing. After January

1920 constant cough with expect. Nursed in the Väsby Hospital $^{16}/_{2}$—$^{30}/_{4}$ 1920 with the diagnosis of bronchitis. On $^{14}/_{1}$ 1923 acutely ill, fever, shiverings. Stabbing pain in left side, dyspnea. Admitted to the Väsby Hospital $^{16}/_{1}$. Diagnosis: tbc. bas. pulm. dx. with fever, gradually lowered.

Admitted to the Sanatorium $^{5}/_{2}$. *Status:* Deviatio septi nasi, hypertroph. concæ med. sin. For the rest 0.

Local status: D 3 over both lungs, except in lower front part of right side. Submetallic R over both lungs, except in the above-mentioned place. Respiration of slightly bronchial character in the upper halves of both lungs. Constitution good, flesh spare. Slight cough with rather inconsiderable expect. Stabbing pain, breathlessness. Appetite, sleep and digestion good. For the rest subjectively well.

Extracts from records. $^{26}/_{3}$ R fewer. Otherwise as before. $^{7}/_{5}$: Right lung, no R anteriorly; D and respiration as before; left lung, fewer R anteriorly. $^{2}/_{6}$: Feels well, out of bed without fever from this day.

Summary: Case of Stage III. without definite cavities (neither in clinical examination nor with Roentgen rays) and without fever; steadily improving.

Weight chart.	Quantity of sputum.
$^{7}/_{2}$ — 66.5 kg.	$^{6}/_{2}$ — 40 ccm.
$^{15}/_{2}$ — 67.5 »	$^{15}/_{2}$ — 30 »
$^{1}/_{3}$ — 68.5 »	$^{2}/_{3}$ — 40 »
$^{14}/_{3}$ — 69.5 »	$^{16}/_{3}$ — 50 »
$^{31}/_{3}$ — 70 »	$^{1}/_{4}$ — 30 »
$^{14}/_{4}$ — 72 »	$^{15}/_{4}$ — 30 »
$^{1}/_{5}$ — 72.5 »	$^{1}/_{5}$ — 45 »
$^{15}/_{5}$ — 73 »	$^{15}/_{5}$ — 30 »
$^{1}/_{6}$ — 73 »	$^{1}/_{6}$ — 15 »
$^{15}/_{6}$ — 73 »	$^{15}/_{6}$ — 25 »
$^{20}/_{6}$ — 74.5 »	$^{1}/_{7}$ — 25 »

Conclusion for Couple a: The case with orange treatment has had the less favourable progress.

Couple b.

3. Or.

Albert Nicolaus B-g, born $^{20}/_{9}$ 1887.

Anamnesis. Pat. $^{4}/_{7}$. No. 1 died of tbc. pulm. at the age of 19 in 1900. No. 3 died of tbc. osteomyelit. at the age of 16 in 1901. — In 1913 period of coughing for some months. Otherwise well till the autumn of 1918, then infl. ep. with relapse. Cough with expect. at least since March 1921. Since beginning of November 1921 constant cough. No hemoptysis? Was then taken ill, with stabbing pain in left side, fever. Not continuously in bed. Appetite bad; night-sweat. Tbc. pulm. stated in March 1921. Abusus aethylicus going on for a long time past.

Admitted $^{28}/_{11}$ 1921. *Status* $^{25}/_{11}$: Constitution good. Flesh somewhat spare. Moderate cough with moderate expect. No breathlessness. Appetite good. Right lung, D 3 scl-II, resp. there br. — br. ves.; hard R, a few—several, partly submetallic. Behind, ssp D 3, ssp to A, D 2—D 1, resp. weak, unclear and br. ves. R, same as in front. Left lung, corresponding parts D 1, resp. harsh, unclear, no R.

Weight:	Bacilli:
$^{25}/_{11}$ 1921 — 69.5 kg.	$^{11}/_{12}$ 1921 +
$^{28}/_{2}$ 1923 — 56.5 »	$^{6}/_{3}$ 1922 +

Pat. not weighed during the orange period.

Extracts from records. Progressing steadily downwards till $^{9}/_{2}$ 1923. Cough about the same as before. Expect. at times increased (more than 200 ccm.), almost purulent. Continuous pain on both sides anteriorly. General condition worse. Status of lungs: over the greater part of both lungs resp. br., D 3 and metallic R. On $^{2}/_{3}$ orange. $^{27}/_{3}$: During last weeks diarrhea, abdominal pains. Attacks of dyspnea, weak pulse. Obj.: metallic R diffusely over both lungs. The last two days abdomen continuously distended, violent abdominal pain; vomiting, not faecal. Excessive tenderness diffusely all over the abdomen. Pulse very slight, quick; cold extremities. † $^{27}/_{3}$.

Temper. about 38° till Jan. 1922, afterwards 38—40,4°; from $^{11}/_{2}$—$^{25}/_{3}$ again about 38°.

Summary: Case in Stage III. with destruction of both lungs. Continually declining before the orange diet was begun. A week afterwards symptoms of tuberculous enterocolitis with supervening peritonitis.

4.

Bror Jakob Harry M-n, born $^{25}/_{9}$ 1900. Upholsterer, Vaxholm.

Anamnesis. Pat. $^{3}/_{4}$. No. 4 has had pleuritis. An uncle tbc pulm. 1919 the pat. had infl. ep. without complications. Enrolled for conscription in the spring of 1919, allowed respite on account of feeble constitution. Began military service in 1921. Well till beginning of April 1922, then cough and expect., since continued. Hemoptysis (about a table-spoonful) in July and Sept. 1922. In bed with fever up to 40° C. during April—May 1922. A physician stated bronchopneumonia. Afterwards about and in work again till Aug. 1922; in July a physician stated tbc. pulm. Temperature not taken for some time. Earlier night-sweat. Appetite generally good. Slight loss of flesh. Never pleuritis.

Admitted $^{11}/_{12}$ 22. *Status* $^{15}/_{12}$: Constitution somewhat feeble. Flesh spare. Coughs slightly with moderate expect. Appetite good. Digestion and sleep good. Feels well. Pulse: 96.

Local status: Upper halves of both lungs D 3, resp. on right side feeble, unclear, on left side br. ves. R on the right some—a few, medium—finer, posteriorly submetallic, anteriorly hard; R on the left some—a few, medium, submetallic. Both lower halves D 1—D 2, more on the right side, resp. there not quite clear, on left side ves. No R.

Extracts from records. $^{3}/_{1}$ 23: Resp. everywhere as before. D increased posteriorly in the bases. Slight cough with perhaps increased expect. Hemoptysis once since last examination (about 90 gr.). $^{26}/_{1}$: Since $^{15}/_{1}$ sensation of stabbing pain on the right side with rising temperature. Much increasing D over the right side base with hardly audible resp. Test puncture $^{22}/_{1}$. Result a somewhat turbid exudate. Tbc bacilli $^{14}/_{12}$ +. *Local status* $^{26}/_{1}$: Left lung. R. audible all the way down both anteriorly and posteriorly, some—a few, medium, hard, in the upper half partly metallic; below A mixed with friction sounds. Resp. and D = $^{8}/_{1}$. Right lung, below A D 2 increasing downwards to absolute; three fingers' breadth below A to the limit of the lung resp. almost 0. Just above, occasional friction sounds. The rest = $^{8}/_{1}$. Cough during the last 24 hours trying, with inconsiderable expect. Feels fairly well. General condition as before. $^{9}/_{3}$: R in left lung and in upper half of right lung more metallic. In lower halves of both lungs friction sounds here and there (remains after ex. pleurit.). Cough and expect. as before. Feels well. Continuously in bed with fever. Condition of health declining. (Prognosis: mala.) $^{12}/_{4}$ status of lungs: 3 big cavities, one in the upper, one in the lower part of right lung; one cavity in the middle of the left lung. Cough and expectoration as before. General condition worse. Feels better than before! $^{1}/_{5}$: Since the last examination the general condition has declined steadily. During the

last days coarse partly metallic R diffusely over both lungs. All the right anterior side sibilant br. resp., metallic in the lower half. Since a few days intensely fetid, abundant sputa. In the last days pulse quick. Very slight dyspnœa. † 1/3.

Weight 11/12 1922 55 kg. Since then not weighed. Occasional traces of alb. During the last 4 months or more, remittent fever from 37—39° C: the last fortnight with more than 3 degrees' variation a day.

Summary: Case in Stage III. with great virulence. In upper halves of both lungs incipient destruction. Quick progress towards death with large destruction setting in.

Conclusion for Couple b: In Case 3, the lessening of the power of resistance through aethylism seems to have been conducive to the progress of the disease. In Case 4, similar progress.

Couple c.

5. Or.

Karl Erik B-g, born 18/8 1902. Farm-owner's son. Väddö.

Anamnesis. Pat. 5/8. One brother died of tbc. pulm. In 1918, after infl. ep. periods of cough, constant fatigue. Cough and expect. after Oct. 1920; stabbing pain in left side. Physician diagnosed pleurit. sicca sin. and tbc. pulm. in Dec. 1920. Nursed in the Serafimerlasarettet, Dec. 1920. Attempts at Forlanini. Nursed in the Hålahult Sanatorium 14/3 1921—19/6 1922. Was out of bed there, without fever, all the time. Forlanini attempts with negative result. Hemoptysis 1/2 litre in Aug., the same in Oct. 1921. Appetite bad, almost continual loss of flesh; since 1920 in all 10 kg.

Admitted 15/12. *Status* 19/12: Constitution fairly good, flesh spare, moderate cough with moderate expectoration. Appetite fairly good. Other organs 0. Status of lungs: Chiefly affected on the left side. Right lung D 1 and D 2 in the apex, resp. unclear, interscapular R anteriorly and posteriorly. Left lung, all D 3, R metallic covering the resp. sounds.

Extracts from records. 27/1 23: On the whole the same status of lungs. R possibly somewhat lessened. Feels well. Less cough with less expect. 1/2 an orange a day. 10/3: No R anteriorly on right side, appetite better (subj.), been out of bed without fever since then. Pleuropericarditis (slight symptoms) as when admitted. 20/4: Local status unchanged. Cough inconsiderable, feels much better, but has not put on flesh. Bacilli all the time. Temperature afebrile all the time. Forlanini attempts without any marked effect on 26/5. Afterwards status quo in the lungs.

Weight chart:

1/3 — 70 kg.	15/4 — 70 kg.	1/6 — 68.5 kg.
15/3 — 70 »	1/5 — 70 »	15/6 — 67.5 »
1/4 — 70 »	15/5 — 68.5 »	30/6 — 68 »

Quantity of sputum:

1/3—15/5 — 90 ccm.
1/6—15/6 — 50 »

Summary: Case in Stage III., practically one-sided, with cavities on the left side. After orange diet, local status improved on both sides, also appetite improved.

6.

Nils Bertil B-n, born 16/11 1906. Errand-boy. Spånga.

Anamnesis. Pat. 3/8. No tbc. in the family. Well till 1919, when infl. ep. Coughing in wintertime for a couple of years. Constant cough with expect.

in the autumn of 1922. Never hemoptysis. Last week night-sweat. Tbc. pulm. diagnosed in Jan. In the Mörby Hospital $^{17}/_{1}$—$^{18}/_{2}$. Two Forlanini attempts there, 100 and 160 ccm. Thin, but not losing flesh.

Admitted $^{22}/_{2}$ 23. *Status:* Constitution lank. Habitus phtisicus. Flesh spare. Coughs slightly with inconsiderable expect. Appetite, digestion, sleep good. *Local status:* Right lung, D 1 and D 2 in the apex, resp. unclear. No R. Chiefly affected on the left side. Left lung, upper half D 3, the rest D 2. Resp. of slightly bronchial character in the apex. Otherwise enfeebled and unclear. R metallic in the apex. Smaller changes than Case 4, but on the whole similar. Other organs 0. Roentgen $^{27}/_{2}$: All the left lung completely filled with foci. Small cavities at the top. Pneumo-thorax treatment continued (up to 500 ccm.). Apex adherent.

Extracts from records. $^{1}/_{3}$: Continued decline. Appetite lessened. R occurring in right lung — gradually progressing. Temp. afebrile. Bacilli found before admittance, but not at Väsby till $^{27}/_{3}$.

Weight chart:

$^{22}/_{2}$ — 63 kg.	$^{14}/_{4}$ — 66.5 kg.	$^{1}/_{6}$ — 65.5 kg.
$^{1}/_{3}$ — 63.5 »	$^{1}/_{5}$ — 67.5 »	$^{15}/_{6}$ — 66.5 »
$^{14}/_{3}$ — 64 »	$^{15}/_{5}$ — 66.5 »	$^{30}/_{6}$ — 66 »
$^{31}/_{3}$ — 66 »		

Quantity of sputum:

$^{23}/_{2}$ — 5 ccm.	$^{4}/_{3}$ — 30 ccm.	$^{1}/_{5}$ — 5 ccm.
$^{24}/_{2}$ — 10 »	$^{10}/_{3}$ — 15 »	$^{15}/_{5}$ — 15 »
$^{25}/_{2}$ — 15 »	$^{1}/_{4}$ — 10 »	$^{1}/_{6}$ — 30 »
$^{26}/_{2}$ — 15 »	$^{15}/_{4}$ — 10 »	$^{15}/_{6}$ — 30 »
$^{2}/_{3}$ — 30 »		

Summary: Case of Stage III., practically unilateral, with cavities on the left side. Grown worse during the stay in the hospital.

Conclusion for Couple c: The orange case has progressed more favourably.

Couple d.

7. Or.

Frans August H-g, born $^{14}/_{10}$ 1870. Married, joiner. Spånga.

Anamnesis. Pat. $^{2}/_{3}$. Sister died of tbc pulm., 40 years ago. Stepmother died of tbc. pulm. Has 7 half-brothers and -sisters; 2 of them died of tbc. pulm. Married since 1898. Five children, one of them died with sequelae of pertussis. Always well till 1918, then infl. ep.; in bed with high fever for a week, did not summon a physician. Cough and expect. Sept. 1921. Underwent operation in the middle of March 1922 for abdominal tumour (not ca.). Shortly before, tbc. pulm. has been stated. After this nursed in the Serafimerlasarettet for pneumonia bilat. $^{27}/_{2}$—$^{24}/_{5}$ 1922. Appetite bad since 4 to 5 years back. Losing flesh. Fever from the middle of March to July 1922.

Admitted $^{12}/_{12}$ 22. *Status* $^{30}/_{12}$: Constitution perhaps somewhat weak. Flesh spare. Inconsiderable cough and hardly any expect. No stabbing pain; breathlessness when moving. Appetite now fairly good. Digestion and sleep fairly good. Feels rather well. Cor: dull sounds. Syst. accompaniments over aorta? For the rest 0. *Right lung*, Scl-I and Ssp D 1, resp. not quite clear. IV—VI D 3, resp. weak, unclear. R laterally from the mammilla and downwards, isolated to a few medium hard. Below A D 3, resp. enfeebled, unclear, slightly bronchial in the depth. *Left lung*, upper part to III and rather more than $^{1}/_{2}$ A D 3—2, diminishing downwards, resp. br.-ves. R in these

areas some—a few, medium—finer, hard. In the lower part resp. very harsh, unclear. Bacilli not examined, as 0 exp. $^{22}/_{12}$ 22 and $^{14}/_{5}$ 23.

Extracts from records. $^{1}/_{3}$: In the left apex only occasional R. Otherwise 0. Right lung, accompaniments diminished. Otherwise as before. Hardly any cough, feels fairly well. $^{2}/_{3}$: an orange a day. $^{15}/_{3}$: Resp. and D everywhere as before. R in toto considerably diminished, in extension as well as in number and degree. $^{27}/_{3}$: Accompaniments are heard only in the right lung below A isolated — a few, finer, and in the left lung I—II. Almost no cough at all. No expect. Feels well. Appetite about as before. $^{14}/_{5}$: Status of lungs = $^{27}/_{4}$. Coughs occasionally with hardly any expect. Fells well. Appetite the whole time, and especially of late, excellent. Has been afebrile. Discharged on $^{15}/_{5}$.

Summary: Case in Stage II. to III., which locally and generally has considerably improved.

Weight chart.:

$^{16}/_{12}$ — 57 kg.	$^{15}/_{2}$ — 61 kg.	$^{15}/_{4}$ — 63.5 kg.
$^{30}/_{12}$ — 57 »	$^{1}/_{3}$ — 62 »	$^{1}/_{5}$ — 64 »
$^{18}/_{1}$ — 59 »	$^{15}/_{3}$ — 62.5 »	$^{15}/_{5}$ — 64.2 »
$^{1}/_{2}$ — 60 »	$^{1}/_{4}$ — 62.5 »	

8.

Sven N-n, born $^{15}/_{8}$ 1875. Night-watchman. Huvudsta.

Anamnesis. Pat. $^{3}/_{2}$. 4 children. Generally well till the spring of 1919, then infl. ep. followed by bronchitis; in bed for two weeks. Since then sometimes cough with inconsiderable expect. $^{15}/_{9}$ 21 hemoptysis (about $^{1}/_{2}$ litre). Physician diagnosed tbc. pulm. Appetite fairly good. No loss of flesh.

Admitted $^{21}/_{2}$ 23. *Status* $^{24}/_{2}$: Constitution fairly good. Flesh spare. Height 180 cm. Weight 72 kg. Slight cough in the morning. No stabbing pain, no breathlessness. Appetite good, bowel sluggish. Sleep fairly good; feels well.

Local status: Right lung, scl-II and ssp-A D 1. Resp. weak, unclear. In the base resp. unclear; a few finer hard R. Left lung, scl—IV D 2, ssp—A D 2. Resp. weak, unclear; isolated — a few fine hard R; in the base resp. not quite clear. Pharynx and larynx show diffuse redness.

Extracts from records. $^{7}/_{3}$: Nowhere R or accompaniments. Coughs unfrequently, almost without expectoration. Feels well. $^{19}/_{3}$: Nowhere R or accompaniments. Never coughs, no expect. Feels well. Bacilli looked for $^{27}/_{2}$, $^{15}/_{3}$, and $^{10}/_{4}$, without being found. Temperature afebrile.

Weight chart:

$^{21}/_{2}$ — 72.5 kg.	$^{1}/_{4}$ — 77 kg.	$^{15}/_{5}$ — 80 kg.
$^{1}/_{3}$ — 74.5 »	$^{15}/_{4}$ — 78.5 »	$^{22}/_{5}$ — 82.2 »
$^{15}/_{3}$ — 76 »	$^{1}/_{5}$ — 78 »	

Summary: Case in Stage I.—II. Locally and generally improved.

Conclusion for Couple d: Both considerably improved, the orange case most.

Couple e.

9. Or.

Josefina A-k, born $^{5}/_{9}$ 1879. Wife of a filer.

Anamnesis. Pat. $^{1}/_{1}$. Well till 1905, when diphtheria. In 1919 pneumonia sin. after infl. ep. Nursed 3 months in the Serafimerlasarettet. Con-

tinuous cough and expect. since May 22. In July the same year hemoptysis (about 1 table-spoonful). Physician stated tbc. pulm. Then 1 month in bed with fever up to 39° C. In September another period of heightened temperature up to 38° C. No night-sweat. Appetite generally good. Lost 4 kg. since last July.

Admitted $^{18}/_{1}$ 23. *Status* $^{21}/_{1}$ 23: Constitution and flesh fairly good. Coughs moderately with inconsiderable expect. Occasionally stabbing pain in left side. Breathlessness when moving. Appetite, digestion, sleep, fairly good. Feels rather well.

Right lung: D 2 in scl-III, ssp—A. Resp in upper parts harsh, unclear, below III. and A harsh, prolonged expirium. R scl—II and ssp—A, a few finer hard R, mixed with rhonchi. *Left lung:* D 1—D 2 in the apex with resp. harsh, unclear, D 3 from $^{1}/_{2}$ A and downwards anteriorly; here resp. enfeebled, unclear, posteriorly br.-ves. Lower half of left lung, R hard, medium, some—a few.

2/3: an orange daily.

Weight chart:

$^{18}/_{1}$ — 70 kg.	$^{15}/_{3}$ — 73.5 kg.	$^{1}/_{5}$ — 76.5 kg.
$^{1}/_{2}$ — 72 »	$^{31}/_{3}$ — 74 »	$^{15}/_{5}$ — 77 »
$^{15}/_{2}$ — 72 »	$^{14}/_{4}$ — 75 »	$^{29}/_{5}$ — 79 »
$^{1}/_{3}$ — 73.5 »		

Extracts from records. $^{4}/_{3}$ Right lung, no R. Left lung as before. Cough and expect. about as before. Feels well. $^{15}/_{4}$ Right lung, no R. Left lung anteriorly no R. Laterally to the left and $^{1}/_{2}$ A all the way down a few hard R. Dry cough sometimes. Feels well. Temp. afebrile. $^{29}/_{5}$ Resp. and D everywhere as before. Left lung, anteriorly no R, posteriorly to the right isolated R in different places interscapularly. Right lung, ssp and downwards isollated hard R; anteriorly Scl—II = posteriorly. Coughs sometimes, without expect. Feeling well. No Roentgen ex. $^{30}/_{5}$. Discharged.

No tbc bacilli found $^{20}/_{1}$, $^{30}/_{1}$, $^{14}/_{2}$, $^{3}/_{5}$, $^{15}/_{5}$.

Summary: Case in Stage III. Left lung more gravely attacked, without sure destruction. Locally and generally, considerable improvement.

10.

Maria Valborg L-n, born $^{29}/_{12}$ 1889. Wife of game-keeper, Nacka.

Anamnesis. Pat. $^{3}/_{10}$. Married since 1905. A cousin tbc. Three children $1^{1}/_{2}$—7 years. Nervous debility when growing up. In 1913 nursed in the Sabbatsberg Hospital for renal hemorrhage during 19 days. Tired in the mornings, but otherwise well, till 1921, when bronchial catarrh. Afterwards periods of cough and expect., at times blood-imbibed sputa. Temp. during the last months on the verge of subfebrile. Appetite fairly good. Hardly any losing of flesh. After partus in July 1922 affection of apex was suspected by physician. Sanatorium treatment was advised in October.

Admitted $^{2}/_{2}$ 23. *Status:* $^{6}/_{2}$ Constitution and flesh good. Coughs occasionally with hardly any expect. No stabbing pain. No breathlessness. Appetite, digestion, sleep good. Feels well. Pharynx and larynx: inconsiderable diffuse redness, mucous coating.

Local status: Right, scl sunk, resp. enfeebled, unclear, in both apices scl—II, D 1—D 2, more on left side. No R. Left, below II. anteriorly and posteriorly resp. everywhere weaker than in the right lung.

Extracts from records. $^{20}/_{2}$ Roentgen ex. shows slight changes, peribronchitic shadows possibly too dark on left side. $^{20}/_{3}$: Nowhere R or accompaniments. Coughs sometimes with inconsiderable expect. $^{4}/_{5}$: Lung status as

before. Never coughs. No expect. Feels well. Temp. afebrile. No bacilli found in examinations $^{14}/_{2}$, $^{13}/_{3}$, $^{10}/_{4}$, and $^{3}/_{4}$.

Weight chart:

$^{3}/_{2}$ — 66 kg.	$^{15}/_{3}$ — 71 kg.	$^{15}/_{4}$ — 73 kg.
$^{15}/_{3}$ — 68 »	$^{1}/_{4}$ — 71 »	$^{1}/_{5}$ — 73.5 »
$^{1}/_{3}$ — 70 »		

Summary: Case in Stage I.—II., with good general condition. Lung status not changed; general condition, good on arrival, still somewhat improved.

Conclusion for Couple e: Case 9 has larger extent than Case 10, but virulence and conditions seem to be similar. Greater improvement of the orange case.

Couple f.

11. Or.

Elsa Elis. S-m, born $^{17}/_{9}$ 1894. Bookbinder, Sundbyberg.

Anamnesis. Pat. $^{1}/_{3}$. No tbc in the family. Morbilli at the age of 5 with bronchitis and eye complications. Since that time often suffering from colds. Otherwise well till Oct. 1919. Afterwards weakly, tired, sometimes febrile. Cough and expect. after this time. No hemoptysis, periodically fever since Nov. 1920, night-sweat, emaciation, appetite constantly bad since a year back. During alternate periods sluggish bowels and diarrhea. No menses since 2 months back. Physician stated tbc. in Nov. 1920. Nursed in the Sundbyberg almshouse in May 1922. There thrombophlebitis.

Admitted $^{30}/_{9}$ 22. *Status:* Constitution fairly good, flesh beneath the average, moderate cough with abundant expect. Breathlessness. Appetite fairly good.

Lung status: The upper halves of both lungs D 3, br. resp. and metallic R, the lower parts resp. harsh, unclear, no R. Right lung posteriorly with weak D 1. Larynx: the right vocal chord and ventricular ligament slightly reddened. Other organs 0. Pulse 100.

Weight chart:

$^{1}/_{3}$ — 53.5 kg.	$^{14}/_{4}$ — 54 kg.	$^{1}/_{6}$ — 55 kg.
$^{15}/_{3}$ — 53.5 »	$^{1}/_{5}$ — 54.5 »	$^{15}/_{6}$ — 54.5 »
$^{21}/_{3}$ — 53 »	$^{15}/_{5}$ — 54.5 »	$^{20}/_{6}$ — 54 »

Quantity of sputum:

$^{1}/_{3}$—$^{1}/_{6}$ — 100 ccm.	$^{15}/_{6}$ — 80 ccm.	$^{20}/_{6}$ — 80 ccm.

Extracts from records. $^{15}/_{12}$: Lung status idem. $^{26}/_{1}$: diffuse bronchitis. $^{2}/_{3}$: An orange daily. $^{9}/_{3}$: Lung status idem. Bacilli $^{2}/_{11}$ +. No bacilli found $^{10}/_{4}$ and $^{20}/_{4}$. $^{23}/_{4}$: R somewhat lessened, everything else idem. Larynx: the right vocal chord and ventricular ligament infiltrated, a small granulation on the back wall. Appetite relatively good. Bowels irregular, sometimes diarrhea. $^{3}/_{6}$: R in toto somewhat lessened, especially anteriorly on the right side. Otherwise as $^{20}/_{4}$. General condition improved in spite of symptoms from the bowels the whole time; larynx the same. Temp. constantly subfebrile. Cough minimal.

Summary: Case in Stage III. Cavity symptoms in the upper halves of both lungs; when admitted inconsiderable symptoms from larynx and the bowels, thrombophlebitis not quite gone. Much improved during the orange diet.

12.

Axelina Maria L-n, born $^{14}/_{12}$ 1895. Servant girl. Lidingön.

Anamnesis. Pat. $^{1}/_{8}$. Tbc. in the family. Served, when 17 years old, in a family where there was a case of manifest tbc. Has a healthy, 3 years old child. In 1919 after infl. ep. weakly. Coughed, had expect., sometimes blood-imbibed. Partus in April. Nursed in St. Erik's Hospital in June 1919, in the Söderby Hospital Oct. 1919—Febr. 20. Out of bed without fever till May 22. Nursed for ileus in the Serafimerlasarettet in May 22. Afterwards again cough, expect. and fever up to 39° C. After op. the whole time bad appetite and night-sweat. Tbc. stated in April 1919.

Admitted $^{20}/_{10}$ 22. *Status:* General condition without remark, flesh spare. Troublesome cough with abundant expect. Breathlessness. Appetite rather bad. Bowels often irregular; pain and often nausea, sometimes diarrhea. Pulse 100. Other organs 0.

Local status: In the upper right and lower left parts D 3, br. resp. and metallic R. Otherwise on the right below, feeble, unclear resp. In the upper left part, D 2 and hard, not metallic R.

Extracts from records. $^{11}/_{12}$: R slightly lessened, cough troublesome as before. $^{23}/_{1}$: Resp. br. also in the upper left parts with a few metallic R. $^{6}/_{3}$: Status idem. Cough troublesome, increased expect. Feels tired. Loss in weight. $^{18}/_{4}$: Status quo. Increased expect. No symptoms from the bowels. General condition less satisfactory. $^{31}/_{5}$: R on right lung somewhat increased. R also below A. R metallic all over the left lung. General condition worse.

Weight chart:

$^{1}/_{3}$ — 47.5 kg. $^{5}/_{3}$ — 47 kg. $^{31}/_{3}$ — 45.5 kg.

Quantity of sputum:

$^{1}/_{3}$ — 100 ccm. $^{15}/_{4}$ — 300 ccm. $^{15}/_{5}$ — 350 ccm.
$^{15}/_{3}$ — 250 » $^{1}/_{5}$ — 300 » $^{30}/_{6}$ — 300 »
$^{1}/_{4}$ — 300 »

Summary: Case in Stage III. with complications from larynx and bowels. Cavity symptoms in all the left lung and in upper parts of the right lung. Generally and locally declining.

Conclusion for Couple f: The orange case shows the more satisfactory progress.

Couple g.

13. Or.

Emilia Josefina K-n, born $^{11}/_{8}$ 1896. Housekeeper. Tureberg.

Anamnesis: Pat. $^{7}/_{10}$. No tbc. in family. Well till 7 years ago when fatigue set in. Examined and nursed for a few weeks in the Väsby Hospital for catarrh in the left apex. Cough and expect. in periods since Jan. 1922. Once blood-imbibed sputa. Appetite generally good. Lost flesh during the last 2 years. Fever since 3 weeks back, 38—40° C. Night-sweat.

Status $^{24}/_{9}$: General constitution without remark. Flesh spare, moderate cough with moderate expect. No stabbing pain, no obvious breathlessness. Appetite, sleep, digestion good, feels a little tired; frequent and abundant menses. Pulse 92.

Right lung: D 1—D 2 in the upper half, resp. unclear, harsh, R isolated, finer. *Left lung:* D 3 in rather more than the upper half, to III and near A, with br. resp. and metallic R. Below D 1—D 2, resp. anteriorly enfeebled,

posteriorly unclear. R in the first-mentioned area some—several, medium—coarse, submetallic—metallic; about A and laterally R isolated finer, hard.

Extracts from records. 5/10: Roentgen. Left lung almost filled with small indurations (tbc.—looking foci). Right lung: from hilus laterally, mostly downwards, similar foci, but not so close together. In the left apex a few small cavities. 13/10: Attempts at pneumothorax on left lung, without effect. 4/11: Right lung, upper half, irregular accompaniments. Left lung, about the same as before. The first successful insufflation (I) on the left side. 7/11: II insufflation. 8/11: III insufflation. 11/11: IV. 15/11: V. 20/11: VI.

Bacilli: 25/9 ++. 5/12 +. 27/4 +. 27/5 ±.

Weight chart:

21/9 — 55.5 kg.	1/12 — 56 kg.	15/2 — 58 kg.	14/4 — 58 kg.
30/9 — 56.5 »	15/12 — 57 »	1/3 — 57.5 »	1/5 — 58 »
14/10 — 56.5 »	30/12 — 56 »	15/3 — 57 »	18/5 — 58 »
1/11 — 57.5 »	1/2 — 57 »	31/3 — 57 »	1/6 — 57.5 »

20/11: laterally in the upper part of right lung a large tbc focus (Roentgen rays), not compressed.

24/11: VII.; physical signs as before. 27/11: VIII. 4/12: IX. 9/12: X.

Roentgen: »Left lung: laterally in lower half pneumothorax rather large. No exudate. Right lung: tbc foci as before.» Physically the lower half lat. no resp., no R. For the rest everywhere resp. audible and a few medium R. Right lung: in some places isolated accompaniments.

13/12: owing to the delicate state of the patient no insufflations have been undertaken. The temperature has risen to 39—40° C. R audible all over the right side anteriorly, in the upper half posteriorly. R extended over right lung, in spite of partial pneumothorax. 8/1 23: over the upper part of both lungs D 3 down to IV on the right, VI on the left and A posteriorly, resp. more or less br. over the scapulae with bronchophony. R metallic. Cough somewhat lessened but with increased expect. General condition as before. 23/1: right lung anteriorly I—III resp. almost br. Left lung anteriorly I—III resp. amphoric, posteriorly R metallic all the way down. Lung status otherwise as on 8/1. Purulent, somewhat increased expect. Since 21/2 rising temperature up to nearly 40° C, now again sinking. General condition improved. 2/3: an orange a day. 5/4: right lung, R, some, medium, are heard over the whole anterior area and ssp to near A. Left lung, R in toto somewhat diminished. Otherwise as on 8/1. Feels very much better than before. Temp. subfebrile, more steady. Somewhat less cough with less expect. 19/5: Right lung below IV no R. Otherwise as before, yet resp. I—III with br. touch. Posteriorly as before; iscp resp. with br. touch. Left lung, R in toto lessened. Otherwise same as on 8/1. Cough somewhat easier with plenty of expect. Feels fairly well. General condition as before. In bed during the greater part of the day with subfebrile temp. 1/6: on some places anteriorly a few R I—III, almost metallic. Posteriorly iscp some few, medium, hard R, partly submetallic. Otherwise nothing abnormal. Left lung: R in toto somewhat lessened, especially anteriorly. Otherwise as on 8/1. Cough troublesome with plenty of expect. Temp. during the last month 37.5—38.5. Pulse 84. Sent home at her own request.

Summary: Case in Stage III., with the gravest changes in the upper part of the left lung. Clinical cavity symptoms confirmed by Roentgen examination. Large foci also in the right lung, yet Roentgen rays show no cavity. Partial pneumothorax in the beginning of November, followed by an aggravation especially of local manifestations in the less affected lung; improvement from February, before the orange cure was begun, and onwards during this cure, the patient growing much better, both locally and generally.

14.

Vivi Margit Constance G-t, born $^{25}/_{10}$ 03. Dressmaker. Nynäshamn.

Anamnesis: Pat. $^{1}/_{3}$. No tbc in the family. Often tired and infirm since childhood. Easily catching colds. At the age of 10 operated upon for adenoid. Tbc pulm. bilat. stated in 1917. Autumn 1918 infl. ep. Later on periods of coughing and increased expect. No hemoptysis. Never night-sweat, fever. Appetite generally fairly good. Nursed at the Hålahult Sanatorium $^{23}/_{5}$ 21—$^{23}/_{9}$ 22. Forlanini for 9 months; during this time loss of flesh. Afterwards at home.

Admitted $^{16}/_{12}$ 22. *Status:* general constitution fairly good. Flesh below the average. Coughs moderately with inconsiderable expect. Breathlessness. Appetite, digestion, sleep good. Feels well. Everything else all right.

Local status: the upper halves of both lungs D 3. Resp. br., metallic R. On the left, posteriorly and downwards D 1 with occasional finer R.

Extracts from records. $^{2}/_{2}$: status idem. $^{15}/_{3}$: lung status idem. Feeling well. $^{27}/_{4}$: idem. $^{10}/_{5}$: idem. $^{9}/_{6}$: lung status as on $^{15}/_{3}$. Coughs a little with slight expect. Appetite bad during last month. Temp. afebrile. Tbc bacilli: $^{17}/_{12}$ —; $^{5}/_{1}$ +; $^{5}/_{3}$ — and $^{16}/_{5}$ +.

Weight chart:		Quantity of sputum:	
$^{1}/_{3}$	— 48.5 kg.	$^{1}/_{3}$	— 15 ccm.
$^{15}/_{3}$	— 49.5 »	$^{15}/_{3}$	— 15 »
$^{31}/_{3}$	— 49 »	$^{1}/_{4}$	— 5 »
$^{14}/_{4}$	— 49.3 »	$^{15}/_{4}$	— 5 »
$^{1}/_{5}$	— 49 »	$^{1}/_{5}$	— 15 »
$^{15}/_{5}$	— 48 »	$^{15}/_{5}$	— 15 »
$^{1}/_{6}$	— 48 »	$^{1}/_{6}$	— 15 »
$^{15}/_{6}$	— 47.5 »	$^{15}/_{6}$	— 15 »
$^{30}/_{6}$	— 47.5 »	$^{30}/_{6}$	— 25 »

Summary: Case in Stage III. Cavities in all the left and in the upper right lung. General condition inconsiderably improved. Lung status the same. All the time without fever, has been out of bed.

Conclusion for Couple g: Case 14 is more stationary and has less virulence than Case 13, which shows a greater improvement.

Couple h.

15. Or.

Elin Hildegard S-l: born $^{4}/_{10}$ 1880. Wife of a labourer. Täby.

Anamnesis: No tbc in family. At the age of 19 servant in a house, where there was tbc in infectious stage. Married at 20. Husband alcoholist. 5 children, $2^{1}/_{2}$—9 years. At 21 erythema nodosum.

Hemoptysis, after a year's coughing, early in 1916. Two periods of nursing in the Väsby Hospital, July 1916—Jan. 1917, Dec. 1917—May 1918. The first period: right lung scl D 1—D 2, ssp—A, D 3—D 2; left lung scl—III, D 3—D 2, ssp—A D 1. In these areas numerous small — medium, hard R. The second period: signs of destruction in the upper halves of both lungs.

When dismissed the second time, $^{4}/_{5}$ 18, weight 64.3, sputum + tbc. Since then she has been working continuously and felt fairly well, but with periods of fever, 38—39° C, which has disappeared after a few days in bed. Cough at periods troublesome, sputa often tinged with blood. Lately bad appetite, gripes and nausea. A tbc swelling on the sternum. Operated. Advised renewed sanatorium treatment in May 1922.

Admitted $^{21}/_{12}$ 22. Constitution weakly, very thin. Coughs slightly with inconsiderable expect. No breathlessness; appetite fairly bad. Digestion troublesome, often gripes and nausea. Sleep good, but sweating at night.

Local status: The upper halves of both lungs D 3; br. resp. and metallic R. Pulse 88.

Extracts from records. $^{6}/_{2}$: R rather decreased. $^{1}/_{3}$: one orange a day. $^{21}/_{3}$: left lung considerably improved, less R. Right lung as before. Cough lessened with expect. as before. Digestion now all right. $^{21}/_{5}$: right lung. R only in I—II. The same as before posteriorly. Left lung, anteriorly lessened R, posteriorly the same. Cough, expect. somewhat decreased. Feeling fairly well. Open-air resting, walks. Bacilli $^{22}/_{12}$ and in later examinations +.

Weight chart:		Quantity of sputum:	
$^{1}/_{2}$	— 54 kg.	$^{1}/_{3}$	— 75 ccm.
$^{15}/_{2}$	— 54.5 »	$^{15}/_{3}$	— 75 »
$^{21}/_{2}$	— 54.5 »	$^{1}/_{4}$	— 50 »
$^{14}/_{4}$	— 55 »	$^{15}/_{4}$	— 125 »
$^{1}/_{5}$	— 55 »	$^{1}/_{5}$	— 100 »
$^{15}/_{5}$	— 55 »	$^{15}/_{5}$	— 100 »
$^{1}/_{6}$	— 55.5 »	$^{1}/_{6}$	— 100 »
$^{15}/_{6}$	— 56 »	$^{15}/_{6}$	— 80 »
$^{21}/_{6}$	— 55.5 »	$^{30}/_{7}$	— 80 »

Summary: Case in Stage III. Cavity symptoms in the upper halves of both lungs. Generally and locally improved (generally already before having the orange).

16.

Brita Märta G-n, born $^{17}/_{12}$ 89. Wife of an engine-driver.

Anamnesis: Pat. $^{1}/_{1}$. No tbc in family. Two healthy children. Ulcus ventriculi three times, last time in 1919, nursed in St. Maria's Hospital. Autumn 1918 infl. ep. Nursed in the Sabbatsberg Hospital for salpingitis. Two abortions, in 1919 and Nov. 1922. Pertussis March—April 1920. In May hemoptysis (150 gr.). Slight hemoptysis in May 1922. During a year continuous cough with expect. Breathless, tired. Appetite good all the time. Inconsiderable losing of flesh. No night-sweat. Tbc stated in July 1922.

Admitted $^{9}/_{1}$ 23. *Status:* constitution fairly good. Flesh somewhat spare. Coughs slightly with inconsiderable expect. Slight breathlessness when moving. Digestion troublesome, can not support food; digestion difficult. Sleep good; feeling well. Pulse 90. Other organs without remark (inconsiderable resistance on the left side of the pelvis [salpingitis] + fluor). *Local status:* slight changes diffusely over both lungs, D 1—D 2, changed, nowhere br. resp., in some places isolated hard R.

Extracts from records. $^{23}/_{2}$: At the beginning of the month in bed, temp. risen, stabbing pain in right iscp. Increased cough and expect. Obj. D 3, br. resp. and metallic R in the upper part of the right lung anteriorly and posteriorly. In other places fewer R, otherwise the same. $^{7}/_{4}$: Right iscp, accompaniments not so hard. Coughs occasionally, now without expect. Feeling well. $^{19}/_{5}$: right lung posteriorly again as $^{23}/_{2}$. Left lung, nothing. Coughs hardly ever. No expect. Feeling well. $^{2}/_{6}$: lung status the same, except that laterally on the right there are now numerous fine, medium R. No cough, no expect. Feeling well. Afebrile. Roentgen $^{12}/_{3}$ 22: three cavities in I, II and III, respectively, the largest in III. Pronounced peribronchitic changes. Left lung: from hilus outwards peribronchitis. Bacilli $^{20}/_{3}$ +, $^{10}/_{4}$ and $^{3}/_{5}$ —, $^{14}/_{5}$ +. Temp. afebrile.

Weight chart:		Quantity of sputum:	
1/3	— 65 kg.	1/3	— 15 ccm.
15/3	— 65 »	15/3	— 65 »
31/3	— 66 »	1/4	— 5 »
14/4	— 66.5 »	15/4	— 10 »
1/5	— 67 »	1/5	— 5 »
15/5	— 65.5 »	15/5	— 0 »
1/6	— 68 »		

Summary: Case in Stage II. and soon (before the beginning of the experiment) III. Cough, expectoration, weight and subjective condition improved during this time. Lung status aggravated.

Conclusion for Couple h: Case 16 shows a less good result than Case 15.

Couple i.

17. Or.

Hilda L-m, born 23/3 98. House-maid. Danderyd.

Anamnesis: Pat. 1/10. One brother, No. 5, dead of meningitis. No tbc in family otherwise. Always well till Jan. 22. Caught cold, got fever, in bed for two weeks. Since then continuous cough and expect. Aug.—Oct. 22 slight hemoptyses, 1 tea-spoonful—1 table-spoonful. Physician stated tbc pulm. in Aug. 22. No emaciation. Hoarse since childhood.

Admitted 21/2 23. *Status:* 25/2: constitution and flesh fairly good. Coughs slightly with inconsiderable expect. Appetite, digestion, sleep fairly good. Feels rather well. Cor: systolic accompaniment all over, the max. in the base. Pulm. II acc. Inconsiderable diffuse reddening in the larynx. Vocal cords, nothing. *Lung status:* right lung, scl and ssp D 3, below to II and A D 2. Resp. anteriorly harsh, unclear; posteriorly br. ves.-br. tinge. Below II resp. not quite clear. Isolated accompaniments. In ssp some few submetallic R. Anteriorly in slc—II and posteriorly below sp some few fine hard R. Left lung: scl—II and ssp—well above 1/2 A D 1—D 2, resp. unclear, harsh. Around sp a number of finer, hard R. In scl isolated fine, hard R. Below II and A resp. harsh.

Extract from records: 6/4: right lung anteriorly as before. Posteriorly, R are heard not quite as far as A. Otherwise as before. Left lung idem. Coughs occasionally with inconsiderable, lessened expect. 28/3: lungs, status quo. Coughs occasionally without expect. 4/5: R are only heard on the right 1/2 A—A and on the left in ssp. Otherwise nothing. Resp. and D as before. Coughs occasionally. Hardly any expect. Suspicious of lighter clothing. Strange mind. Eats plenty, good appetite. Wishing to leave. Has got a bed in another sanatorium. Temp. afebrile. Sputum examined 27/3 + and 27/5 —.

Weight chart:

31/1	— 67 kg.	31/3	— 65.5 kg.	15/5	— 65 kg.
1/3	— 67 »	14/4	— 66 »	1/6	— 63.5 »
15/3	— 66 »	1/5	— 65 »		

Summary: Case in Stage III with changes in both apices, trace of destruction on the left. Open tbc. Distinct improvement all the time in spite of decreasing weight. Pharyngolaryngitis chron.

18.

Knut L-g, born 13/1 02. Farm labourer. Adelsö.

Anamnesis: Pat. 8/3. A sister dead of tbc in 1915. Otherwise no tbc in family. Well till Jan. 21, then cough, expect., breathlessness, emaciation

and night-sweat. Temp. not taken. Never hemoptysis. Tbc pulm. stated in May 21. Nursed at Hamra $^{29}/_{8}$ 21—$^{22}/_{7}$ 22. Sometimes in bed with a temperature, generally without fever and about.

Admitted $^{10}/_{10}$ 22. *Status* $^{13}/_{10}$: constitution fairly good, flesh below the average. Sometimes stabbing pain in the right side posteriorly. Breathlessness when moving. Appetite, digestion, sleep good. Feeling well.

Local status: The upper half of right lung and the lower third of left lung D 3, resp. br. ves., harsh, unclear; a moderate number of medium, hard, partly metallic R. Other parts, isolated fine R (catarrhal).

Extracts from records. $^{23}/_{11}$: R in toto diminished. Cough diminished. Expect. as before. $^{3}/_{1}$: left lung posteriorly no R, anteriorly as before. Right lung anteriorly scl—II, resp. pronouncedly br. + bronchophony, posteriorly as before. Cough troublesome. Feeling well. $^{17}/_{2}$: status idem. Cough as before. Expect. somewhat lessened. Feeling well. $^{4}/_{4}$: in bed since some weeks with fever up to 40° C, stabbing pain in right side anteriorly and downward, increased cough. Status: right lung anteriorly D 3, br. resp., especially distinct in I—II, and some medium partly metallic R. Otherwise such R diffusely over the whole lung, mingled with coarse rhonchi. R posteriorly metallic $^{1}/_{3}$ A—A. Left lung: R anteriorly and downwards more metallic than before. Ssp—ang., isolated to some few, medium hard R. Below ang. isolated coarse rhonchi. Cough still troublesome with fairly abundant expect. Feeling tired. $^{17}/_{5}$: nowhere rhonchi. Left lung, some to some few R $^{1}/_{3}$ A all the way down; hard but without distinct consonance. Right lung, generally less consonance of R. Otherwise status idem. Temp. all the time febrile—subfebrile, constantly sinking. Cough and expect. lessened. General condition worse.

Summary: Case in Stage III. with a great change for the worse in lung status and general condition. Subfebrile.

Weight chart:		Quantity of sputum:	
$^{1}/_{2}$	77.5 kg.	$^{2}/_{3}$	75 ccm.
$^{14}/_{2}$	77.5 »	$^{10}/_{3}$	75 »
$^{15}/_{5}$	68.5 »	$^{1}/_{4}$	150 »
$^{1}/_{6}$	70 »	$^{15}/_{4}$	100 »
$^{15}/_{6}$	70 »	$^{1}/_{5}$	75 »
$^{30}/_{6}$	70 »	$^{15}/_{5}$	100 »
		$^{1}/_{6}$	75 »
		$^{15}/_{6}$	100 »

Conclusion for Couple i: The orange case has progressed better.

Couple k.

19. Or.

Augusta Karolina S-r, born $^{2}/_{6}$ 91. Wife of timber-yard labourer. Ingarö.

Anamnesis: Pat. $^{2}/_{7}$. No tbc in family. One child, 15 years, healthy. Since childhood periodically evil-smelling secretion from right ear. Three partus arte prematuri owing to albuminuria. Since 1914 after the last confinement she has felt weakly. Infl. ep. autumn 1918. Afterwards cough and expect. Tbc stated in June 1919. Four small hemoptyses, last time midsummer 1921, a couple of table-spoonfuls. Pneumothorax treatment in the Serafimerlasarettet Oct. 1919—June 1921, interrupted on account of progression in the less affected lung. Nursed in the Serafimerlasarettet June 1922 for hemoptysis. Appetite during the last months bad, emaciation, temp. up to 39° C.

Admitted $^{18}/_{1}$ 23. *Status* $^{22}/_{1}$: Constitution weak; pale, flesh very spare. Cyanosis; breathlessness. Appetite bad; feeling tired. Refuses to eat bread, bread and butter, fruit. Takes much milk and some meat. Otitis med. chron. supp. dx. et sin. c. granulation. Hemoglobin 45 % (Tallquist).

Local status: rather more than half of both lungs from above D 3, resp. br., metallic R.

Extracts from records. $^{5}/_{2}$: R in toto considerably diminished. Feeling very tired. Coughs less, expect. diminished. $^{2}/_{3}$: an orange a day. $^{11}/_{4}$: R considerably diminished, scl —II and ssp—1/2 A. Left lung, posteriorly at the base catarrhal accompaniments. Cough lessened, expect. likewise. Feeling considerably better, but the increase in weight is still unsatisfactory. 55 % hgbl. (Tallquist). $^{30}/_{5}$: catarrhal accompaniments have disappeared, otherwise as before. Cough and expect. still less. »Appetite much better since two months». Consumed earlier almost exclusively liquid food. 65 % hgb. without Fe treatment. $^{20}/_{1}$ no bacilli, after $^{30}/_{1}$ +.

Weight chart:

$^{18}/_{1}$ — 48 kg.	$^{1}/_{3}$ — 48.5 kg.	$^{16}/_{4}$ — 48.5 kg.	$^{1}/_{6}$ — 51 kg.
$^{1}/_{2}$ — 48 »	$^{15}/_{3}$ — 48 »	$^{1}/_{5}$ — 49.5 »	$^{15}/_{6}$ — 51.5 »
$^{15}/_{2}$ — 48 »	$^{31}/_{3}$ — 48 »	$^{15}/_{5}$ — 50.5 »	

Summary: Case in Stage III. with cavity symptoms, which have receded. General and local improvement, to some degree already before the orange was given. Considerably better result than had been expected.

20.

Anna Lovisa A-n, born $^{9}/_{8}$ 1860. Vada.

Anamnesis: Married since 1884. 9 children, one dead at the age of 23 in tbc pulm. 1918. No. 9 has tbc pulm. A granddaughter has tbc pulm. Has had »gastric catarrh» for a long time. Since at least 10 years back constant breathlessness when moving. 1904 pneumonia, nursed in the hospital of this place. Afterwards cough and expect. in periods; constantly since 1918 when she had infl. ep. Nursed here in another department in the spring of 1922 for bronchitis: no tbc bacilli in sputum. Taken violently ill in Oct. 1922 with high fever and bad cough. Blood-imbibed sputa. Afterwards in bed with fever till admitted into the hospital $^{18}/_{1}$. Tbc pulm. then stated.

Admitted into the sanatorium $^{29}/_{1}$. *Status* $^{4}/_{2}$ 23: Constitution fairly good. Flesh spare. Cough moderate with moderate expect. No stabbing pain. Breathlessness when moving. Appetite, digestion, sleep fairly good. Feeling tired. *Right lung:* scl—III D 3, resp. br., some—several medium—coarser metallic R. Likewise in ssp—A. Below anteriorly and posteriorly D 2, resp. unclear, harsh; posteriorly almost br. ves. *Left lung:* Scl—III and ssp—1/2 A D 2, resp. of slightly bronchial character. R I—III and sp—1/2 A some few, fine—medium, hard. Below resp. harsh and unclear. Cor: hypertrophy? Weak systolic accompaniment all over the heart. Pulm. II acc. Pulse 100, somewhat soft.

Extracts from records. $^{19}/_{2}$: Right lung anteriorly only isolated R I—II. Otherwise nothing, posteriorly as before. Left lung, no certain R. Coughs less with less expect. Feeling fairly well. Complaining of breathlessness. Cor: no distinct accompaniment. $^{1}/_{3}$ and $^{14}/_{4}$: examinations with same result. $^{1}/_{5}$: left lung posteriorly no R. Otherwise lung status about the same as on $^{4}/_{2}$. Cough rather troublesome with somewhat increased expect. Feels tired, breathless. Appetite bad. $^{3}/_{5}$: resp. and D everywhere as before; left lung, no R. Right lung posteriorly, resp. br., bronchophony interscapularly. D with

metallic R. Below A resp. br.-ves. with some few hard R intermingled with rhonchi and friction sounds. Right lung anteriorly isolated fine hard R, intermingled with rhonchi. No increase of weight during the last month. Complains of pain in the pit of the stomach, obj. tenderness. Leaves the sanatorium contrary to advice.

Temp. afebrile during the first month, afterwards subfebrile. Last week towards 39°, remittingly. Bacilli examined $^{30}/_{1}$ +, and $^{3}/_{5}$ —. 100—150 ccm. of mucopur. sputum daily.

Weight chart:

$^{1}/_{2}$ — 56.5 kg.	$^{15}/_{2}$ — 60 kg.	$^{14}/_{4}$ — 60 kg.
$^{15}/_{2}$ — 58 »	$^{31}/_{3}$ — 60 »	$^{1}/_{5}$ — 59.5 »
$^{7}/_{3}$ — 59 »		

Summary: Case in Stage III. with beginning destruction in the upper half of the right lung, proceeding to a large cavity. Local aggravation. At first general improvement, afterwards getting worse. (After leaving the sanatorium her condition grew still worse at home, where she had about the same treatment.)

Conclusion for Couple k: The orange case has had the better progress.

Couple l.

21. Or.

Maria Elisabet (*Betty*) *E-n*, born $^{19}/_{11}$ 02. Skipper's daughter. Vätö.

Anamnesis: Pat. $^{6}/_{5}$. Father tbc, youngest child tbc of slight degree. Always delicate. In the autumn 1918 infl. ep. Spring 1919 lymphomata colli, treated with Roentgen in St. Maria's Hospital; now disappeared. Midsummer 1922 hemoptysis, about a coffee-cup. Only after that continuous cough with some expect. Tbc stated in June 1922.

Admitted $^{19}/_{2}$ 23. *Status* $^{23}/_{2}$: constitution and flesh without remark. Coughs slightly, almost without expect. Appetite good. *Local status:* both apices D 2. Resp. changed, a number of rather fine R. $^{3}/_{3}$: an orange a day. $^{6}/_{3}$: R diminished everywhere. D and resp. as before. Bacilli $^{27}/_{3}$: none. $^{10}/_{4}$: no expect. $^{16}/_{5}$: local status idem. Never coughs. No expect.

Summary: Case in Stage II in a stout person with good general condition, which has improved with lung status. Progress better than was expected.

Weight chart:

$^{19}/_{2}$ — 64 kg.	$^{1}/_{5}$ — 66.5 kg.
$^{1}/_{3}$ — 65.5 »	$^{15}/_{5}$ — 65.5 »
$^{15}/_{3}$ — 65 »	$^{1}/_{6}$ — 65.5 »
$^{1}/_{4}$ — 65.5 »	$^{15}/_{6}$ — 66 »
$^{15}/_{4}$ — 66 »	$^{30}/_{6}$ — 65.5 »

22.

Svea Viktoria Elvira A-t, born $^{17}/_{8}$ 07. Daughter of farm labourer. Markims.

Anamnesis: Pat. $^{5}/_{5}$. 9 half-brothers and sisters. No tbc in family. Autumn 1918 infl. ep. Two years later pneumonia. Cough in autumn and spring. Since autumn 1922 increased cough, bad appetite, emaciation. Never hemoptysis. Tbc stated in Jan. 1923.

Admitted $^{31}/_{1}$ 23. *Status:* Constitution somewhat weakly. Flesh spare. Coughs slightly, almost without expect. Appetite not so good. Otherwise without remark. Other organs, nothing abnormal. *Lung status:* in both bases D 2—D 3, resp. in the right base br. ves.; enfeebled on the left, R rather hard and large (rest of pneumonia with bronchial catarrh) D 1—D 2 in both apices, more pronounced on the right. In the right interscap. and scl—I sin. some small hard R.

Extracts from records. $^{25}/_{2}$: R considerably lessened. Status otherwise the same. No expect. Since a fortnight in bed with fever. Obj. posteriorly on the right below A friction sounds = dry pleuritis. Since a week erythema nodosum on both legs and left arm. Temp. sinking. Feels well. No pain. No bacilli $^{14}/_{2}$, $^{2}/_{3}$ and $^{3}/_{3}$. $^{7}/_{5}$: nowhere certain R or accompaniments. Never coughs; no expect. Feels well.

Summary: Starved girl with slight tbc. (Stage I—II). After passing aggravation (pleuritis) pronounced improvement. Temperature afebrile.

Weight chart:

$^{15}/_{2}$	— 48 kg.	$^{1}/_{5}$	— 51 kg.
$^{1}/_{3}$	— 49 »	$^{16}/_{5}$	— 52 »
$^{15}/_{3}$	— 48.5 »	$^{1}/_{6}$	— 54 »
$^{31}/_{3}$	— 47.5 »	$^{15}/_{6}$	— 52.5 »
$^{14}/_{4}$	— 49.5 »	$^{30}/_{6}$	— 53.5 »

$^{1}/_{2}$ and $^{15}/_{6}$ no sputa.

Conclusion for Couple 1: The orange case has had the better progress.

Couple m.

23. Or.

Ida Margit Johanna H-n, born $^{24}/_{3}$ 05. Daughter of an enginge-foreman. Hammarby.

Anamnesis: Par. $^{2}/_{3}$. Father has healed tbc. Otherwise no tbc in family. Felt tired and weak since the spring of 1922. Bad appetite, losing of flesh, breathlessness when moving. No cough or expect. Never hemoptysis. Tbc stated in June 1922 through Roentgen examination in the Serafimerlasarettet.

Admitted $^{5}/_{2}$ 23. *Status* $^{11}/_{2}$: constitution fairly good. Flesh somewhat below the average. Never coughs, no expect. Breathlessness when going upstairs. Appetite, digestion, sleep good. Feeling well. *Local status:* D 1 in apices of both lungs, resp. changed. I dx., br. ves. resp. and isolated fine R. Other organs, nothing.

Extracts from records. $^{3}/_{3}$: an orange a day. $^{25}/_{3}$: nowhere certain R or accompaniments. Coughs occasionally without expect. Feels well. $^{7}/_{5}$: lung status idem = only D 1. Coughs occasionally without expect. Feels well. (Roentgen: small foci in left apex and confluent on the right.) Film on the right apex. Temp. the whole time afebrile. No bacilli $^{1}/_{3}$. $^{15}/_{6}$: no sputa. Dismissed $^{30}/_{6}$.

Weight chart:

$^{1}/_{3}$	— 56 kg.	$^{15}/_{4}$	— 57 kg.	$^{1}/_{6}$	— 58 kg.
$^{15}/_{3}$	— 56 »	$^{1}/_{5}$	— 58 »	$^{15}/_{6}$	— 57.5 »
$^{1}/_{4}$	— 56.5 »	$^{15}/_{5}$	— 58 »	$^{30}/_{6}$	— 58 »

Summary: Case in Stage I., which has progressed to healing.

24.

Hulda Katarina B-y, born $^{30}/_{1}$ 99. Housemaid. Danderyd.

Anamnesis: Pat. $^{3}/_{6}$, twin. Mother has had repeated lung hemorrhages. Always well till Febr. 22; since then constantly tired, coughed up phlegm in the mornings. Hemoptysis, about 100 gr., June 22. Afterwards subfebrile temperature the whole summer. Appetite good all the time. No emaciation. Tbc stated in Sept. 22.

Admitted $^{3}/_{9}$ 23. *Status* $^{6}/_{9}$: constitution and flesh ordinary. Sometimes hawks up a little phlegm in the morning. No cough. Sometimes breathlessness when moving, and palpitation of the heart. Appetite, digestion, sleep good. Feels well. Other organs, nothing. Pharynx, diffuse reddening, mucous coating. Right lung: D 1—D 2 scl—II, ssp—rather more than A, harsh, unclear resp. No R. Otherwise resp. everywhere unclear, in places harsh or enfeebled.

Extracts from records. $^{18}/_{4}$: nowhere R or accompaniments. Never coughs. »Still slight amount of phlegm from the throat.» Feels well. $^{31}/_{5}$: status idem. $^{6}/_{6}$: lungs the same. Departs at her own request. No cough, slight phlegm from throat. Temp afebrile. No extra treatment. No tbc bac. found at examination $^{13}/_{3}$, $^{23}/_{3}$ and $^{26}/_{4}$.

Weight chart:

$^{2}/_{3}$ — 64.5 kg.	$^{14}/_{4}$ — 67.2 kg.	$^{15}/_{5}$ — 67.5 kg.
$^{15}/_{3}$ — 66.5 »	$^{1}/_{5}$ — 67 »	$^{1}/_{6}$ — 68 »
$^{31}/_{3}$ — 67.5 »		

Summary: Case in Stage I—II without R. Lung status unchanged General condition improved. Pharyngit. chron.

Conclusion for Couple m: Both cases show a favourable progress.

Couple n.

25. Or.

Agda Sylvia E-n, born $^{20}/_{9}$ 10. Skipper's daughter. Vätö.

Sister of Maria Elisabet (No. 21). Always well till the autumn of 1918, then light infl. ep. After that reduced hearing. Otherwise felt well. Tbc pulm. stated by physician when her sister fell ill. She had constantly felt tired, however, since a year back. No fever and no night-sweat. No hemoptysis. Appetite good, no emaciation. Had a good home.

Admitted $^{19}/_{2}$ 23. *Status* $^{23}/_{2}$ 23: constitution fairly good. Flesh a little below the average. No cough or expect. No stabbing pain. No breathlessness. Appetite, digestion, sleep good. Feels well. No heart hypertrophy. Systolic accompaniment over the base. II pulm. acc. Pulse 100, normal. *Lung status:* D 1 scl—I on both sides, and on both sides interscap. Likewise D 1 on left side IV—VI anteriorly and at the base posteriorly. Resp. in these parts harsh, unclear. Scl—II on both sides, interscap., and laterally on the left isolated — some few fine, hard R.

Extracts from records. $^{1}/_{3}$: an orange daily. $^{6}/_{4}$: resp. and D everywhere as before. No R. Never coughs. No expect. Feels well. $^{16}/_{5}$: nowhere R or accompaniments. Never coughs. General condition about the same as on admission to the sanatorium. Feels well. Temp. the whole time afebrile. Dismissed $^{17}/_{5}$.

Weight chart:

$^{19}/_{2}$ — 47.5 kg.	$^{1}/_{4}$ — 47.5 kg.	$^{1}/_{5}$ — 47.5 kg.
$^{1}/_{3}$ — 48 »	$^{15}/_{4}$ — 47.5 »	$^{15}/_{5}$ — 47 »
$^{15}/_{3}$ — 48 »		

Summary: Bilateral hilus tbc with objectively distinct improvement. General condition about the same as when admitted to the sanatorium.

26.

Elsa Sofia M-m, born $^{13}/_{7}$ 07. Daughter of a plumber. Södertälje.

Anamnesis: Pat. $^{2}/_{7}$. Both parents have had tbc, mother died at Väsby, father nursed in sanatorium. Brother, No. 1, dead in unknown disease, other brothers and sisters healthy. Otherwise no tbc in family. At the age of 3 in bed for a month, severely ill with fever; since then always easily catching cold and getting cough. Otherwise well till the age of 11; then lymphomata colli, operated at the Södertälje Hospital. Afterwards treated with Roentgen and quartz lamp. Cough without expect. since at least a year. Never hemoptysis. Appetite good, no emaciation. No fever or night-sweat. Tbc pulm. stated in Oct. 22. Home conditions bad.

Admitted $^{26}/_{2}$ 23. *Status* $^{4}/_{3}$: constitution fairly ordinary, rather thin. Coughs slightly without expect. Appetite, digestion, sleep good. Feels well. Lymphomata on both sides of neck and lower jaw. Hypertrophia tonsillar. *Lung status:* Hilus affection, with D 1—D 2 in both interscap. and I—II with small fine R. Resp. harsh and unclear.

Extracts from records. Nowhere R or accompaniments. Never coughs. No expect. Feels well. Incision of purulent lymphoma under the chin. Large quantities of yellowish green, thick pus discharging. Tamponade. An open fistula from lymphoma on the left side of the neck is also secerning. $^{17}/_{4}$: quartz lamp. $^{29}/_{5}$: nowhere R or accompaniments. Never coughs. No expect. Feels well. Still secretion from fistulæ. Temp. afebrile. Sputa: $^{27}/_{2}$ no bacilli; $^{16}/_{6}$ no sputa.

Weight chart:

$^{26}/_{2}$ — 48 kg.	$^{15}/_{4}$ — 48.5 kg.	$^{1}/_{6}$ — 50.5 kg.
$^{15}/_{3}$ — 49.5 »	$^{1}/_{5}$ — 48 »	$^{15}/_{6}$ — 51 »
$^{1}/_{4}$ — 48.5 »	$^{15}/_{5}$ — 49 »	$^{30}/_{6}$ — 51.5 »

Summary: Hilus affection with purulent lymphomata under the chin, which has improved locally in the lungs and possibly also with regard to the general condition.

Conclusion for Couple n: The orange case has progressed somewhat more favourably (?).

Couple o.

27. Or.

Ingrid Karolina R-m, born $^{1}/_{2}$ 99. Wife of shoe-factory workman. Nacka.

Anamnesis: Pat. $^{3}/_{3}$. No tbc in family. Married in May 1921. Nullipara. Healthy till the age of 14, then operated upon for appendicitis. Afterwards feeling weakly. 1919 nursed in hospital for cystitis with inflammation of the kidneys. Well till Dec. 1921, then pain in her throat, difficulty of swallowing, treated with serum by physician supposing diphtheria. The attack passed. Since then well till Aug. 1922, then the same kind of pain in her throat. In the Serafimerlasarettet the physician stated tbc laryngis et pulm. Operated

in larynx $^{5}/_{9}$. Afterwards nursed for a week in the Sabbatsberg Hospital. Cough and expect. since Dec. 21. Often blood-imbibed sputa. Often fever, up to 38° C. Night-sweat. Appetite less good since 1919; emaciation since then.

Admitted $^{5}/_{2}$ 23. *Status* $^{9}/_{2}$: Constitution fairly good. Flesh spare. Pale; coughs slightly with inconsiderable expect. Very breathless when moving. Often palpitation of heart. No longer any pain in throat. Feeling somewhat tired. Cor: slight hypertrophy towards the left. Slight systolic accompaniment all over the heart, strongest over the base. *Lung status:* D 1—D 2 in both scl—II. On the right side posteriorly well down to A, the same D; on the left down to $^{1}/_{2}$ A. In the same areas resp. unclear. Resp. everywhere in the lungs slightly changed (enfeebled, not quite clear, harsh, prolonged expiration). R sparse, small, fine in both I—II and on the left posteriorly about 1/2 A and at A. In larynx on the back wall some infiltration, and epiglottis a little swollen, especially in the left part.

Extracts of records. $^{21}/_{2}$: since a few days periodically palpitation of heart, general restlessness, slight rise of temperature (up to 38), nasal catarrh, headache. No pain in chest. Cor: accompaniments more distinct. Pulm. II more acc., sometimes a grating systolic accompaniment over Pulm. II (superficially?). Lungstatus idem. $^{3}/_{3}$: an orange a day. In the beginning of March in bed with alveolar abscess which was opened and scraped out, tamponade. Looked like tbc pus. Pat. has earlier had some such abscesses. Healing slowly, secretion stopped only in June. $^{23}/_{3}$: nowhere R or accompaniments. Cough lessened with less expect. Feels well. No longer any symptoms from heart. Objectively, no certain accompaniment. Larynx, status idem, but no swelling of the epiglottis. $^{4}/_{5}$: nowhere distinct R, but resp. everywhere unclear. Otherwise as on $^{3}/_{3}$. Cough for the moment somewhat irritating with inconsiderable expect. Last weeks occasional headaches. Last days slight rise of temp. (acute infection of throat).

Weight chart:	Quantity of sputum:
$^{1}/_{3}$ — 50 kg.	$^{1}/_{3}$ — 20 ccm.
$^{15}/_{3}$ — 50 »	$^{15}/_{3}$ — 15 »
$^{31}/_{3}$ — 51 »	$^{1}/_{4}$ — 15 »
$^{14}/_{4}$ — 50.5 »	$^{15}/_{4}$ — 5 »
$^{1}/_{5}$ — 53 »	$^{1}/_{5}$ — 10 »
$^{15}/_{5}$ — 23 »	$^{15}/_{5}$ — 10 »
$^{1}/_{6}$ — 52.5 »	$^{1}/_{6}$ — 10 »
$^{15}/_{6}$ — 52 »	$^{15}/_{6}$ — 10 »

$^{1}/_{6}$: local status, no R, otherwise as before. General condition improved, feeling well. Temp. afebrile. Bacilli examined $^{14}/_{2}$ and $^{14}/_{4}$ = 0.

Summary: Case in Stage II. with diffuse lighter changes over both lungs, bone abscess and larynx affection (pericarditis?). In the anamnesis affliction of kidneys.

Considerable improvement with disappearing of R and larynx symptoms; bone affliction healed. General condition considerably improved.

28.

Maria Charlotta Viveka R-i, born $^{9}/_{7}$ 95. Telephonist 09. Ljusterö.

Anamnesis: Pat. $^{4}/_{4}$. Mother dead of tbc ren. Otherwise no tbc in family. As a child often coughing. Of infantile diseases only morbilli, slight form. Spring 1919 pain in the left renal area and urinary strain. In 1917 pain at urination. Frequent urinations at night. Extirpation of tuberculous left kidney in the Serafimerlasarettet 1918. Autumn 1918 slight infl. ep.

Afterwards fatigue and rise of temp. autumn and spring. Since autumn 1921, slight continuous cough, almost without expect. At one occasion, 8—9 years ago, slight spitting of blood. Temp. during last year with a tendency of rising to 38° when moving. Periodically night-sweat. Appetite at the end of last year bad, now again good. Decreased in weight 3 kg. during the last months. Tbc pulm. stated in Dec. 1921.

Admitted $^{23}/_{2}$ 23. *Status* $^{26}/_{2}$: constitution and flesh good. Coughs occasionally with inconsiderable expect. Appetite good. Gets diarrhea easily. Feels tired at times, but generally well. Larynx slightly reddened diffusely, somewhat hypertrophic tonsilli with a few polyp. nasi sin. *Lung status:* anteriorly scl—III on the right, scl—II on the left, posteriorly ssp on the right, ssp—$^{1}/_{2}$ A on the left D 1—D 2, resp very harsh, unclear. In the lower parts of the lungs resp. harsh. Right lung, I—II and sp—$^{1}/_{2}$ A isolated to a few fine to hard R. Left lung, no R. $^{15}/_{4}$ nowhere R or accompaniments. Coughs occasionally without expect. Generally feels well except at the periods of the menses, when there is often a pain in the right renal region and just above the symphysis on the left side. Urine sometimes a little turbid. $^{6}/_{5}$: no sediment in urine. $^{17}/_{5}$: nowhere R or accompaniment. Resp. less harsh and unclear. D as before. Never coughs. No expect. Feels well. Temp. afebrile. No tbc bacilli.

Weight chart:

$^{23}/_{2}$ — 64 kg.	$^{31}/_{3}$ — 65.5 kg.	$^{1}/_{5}$ — 65.5 kg.
$^{1}/_{3}$ — 65 »	$^{14}/_{4}$ — 65.5 »	$^{15}/_{5}$ — 66 »
$^{15}/_{3}$ — 65,5 »		

Summary: Case in Stage I—II locally and generally improved. Has had kidney complications.

Conclusion for Couple o: The orange case has progressed somewhat more favourably.

Couple p.

29. Or.

Maria Linnea Josefina O-n, born $^{20}/_{10}$ 97. Wife of electrician. Sundbyberg.

Anamnesis: Pat. $^{2}/_{4}$. Two of the other children dead in tbc pulm. Married since 1920. One child, two years old. Always well till April 1922, then pneumonia sin. Afterwards cough and expect. Subfebrile temp. since the same time. Sometimes night-sweat. Tbc pulm. stated in April 1922, when sanatorium treatment was advised. Appetite generally good. No emaciation.

Admitted to the Väsby Hospital $^{3}/_{4}$ 23. Moved to the Sanatorium $^{19}/_{4}$. An orange daily from $^{3}/_{4}$.

Status $^{20}/_{4}$: constitution fairly good. Rather thin. Coughs moderately with moderate expect. Breathlessness when moving. Appetite good. Digestion troublesome, often diarrhea. Sleep bad. Other organs, nothing. *Local status:* all the left lung D 3, upper half resp. br. and submetallic—metallic R, some—some few. Lower part, resp. harsh, unclear, a few hard, medium R intermingled with friction sounds. Right lung: scl, ssp, D 3. I—II and sp—more than 1/2 A, D 1—D 2. Resp. over all this area of br. character. Then all the way down resp. harsh, unclear. Scl—II and ssp—more 1/2 A some few partly submetallic R. Laterally and below A isolated dry accompaniments.

Extracts from records. $^{2}/_{5}$: R in toto diminished. Otherwise equal. Cough and expect. as before. Temp. sinking. General condition improved. Feels well. $^{15}/_{5}$: very much the same.

Bacilli $^{20}/_{4}$ +.

Dismissed home $^{15}/_{9}$. On $^{11}/_{12}$ 23 condition good, subjectively better than when leaving the sanatorium.

Weight chart:

$^{5}/_{4}$ — 66.2 kg.	$^{1}/_{6}$ — 68.5 kg.	$^{1}/_{8}$ — 69 kg.
$^{19}/_{4}$ — 66.5 »	$^{15}/_{6}$ — 68.5 »	$^{15}/_{8}$ — 69.5 »
$^{1}/_{5}$ — 67.5 »	$^{1}/_{7}$ — 69 »	$^{1}/_{9}$ — 69.5 »
$^{15}/_{5}$ — 68 »	$^{15}/_{7}$ — 68.5 »	

Summary: Case in Stage II. praec. sin. with destruction over the upper half of the left lung. Subjectively and objectively improvement.

30.

Ida Albertina Birgitta K-n, born $^{14}/_{10}$ 98. Bookbinder. Sollentuna.

Anamnesis: Pat. $^{2}/_{9}$. Well till Nov. 22, then began to feel tired and weak. Afterwards cough and expect. Hemoptysis a couple of tea-spoonfuls on $^{5}/_{12}$ 22. Appetite generally good. Losing flesh the last months. Since six weeks fever up to 39.5° in the evening, and night-sweat. Tbc stated $^{5}/_{12}$ 22.

Admitted to the Väsby Hospital $^{3}/_{4}$, removed to the Sanatorium $^{13}/_{4}$. *Status* $^{20}/_{4}$: Constitution fairly good. Flesh spare. Coughs moderately with moderate expect. Appetite bad. Digestion troublesome. Diarrhea frequently. Sleep generally good. Feels well. Larynx inconsiderable diffuse reddening. Right ventricular ligament somewhat swollen, reddened. Obj. nothing from abdomen. *Lung status:* right lung scl—II and ssp— not quite A D 3 + br. ves. resp. + some few submetallic R. For the rest all the way down D 1 and resp. very harsh, not quite clear. Left lung: scl D 2—D 3. I—II D 1—D 2. Posteriorly D 3 to 1/2 A. Resp. very harsh, not quite clear. Sp to 1/2 A a few fine hard R.

Extracts from records. $^{1}/_{8}$: right lung, R heard scl—III and ssp—more than $^{1}/_{2}$ A. Left lung: no certain R. Coughs hardly ever. Expect. as before. $^{16}/_{8}$. Status quo. Periodically diarrhea and vomiting. Temp.: febrile—subfebrile. Sputa + tbc all the time.

Weight chart:

$^{19}/_{4}$ — 58.5 kg.	$^{15}/_{5}$ — 59 kg.	$^{15}/_{6}$ — 59.5 kg.
$^{1}/_{5}$ — 58.5 »	$^{1}/_{6}$ — 60,5 »	$^{1}/_{7}$ — 60 »

Summary: Case in Stage III., bilateral with the gravest changes in the upper half of right lung. There trace of destruction. Lung status about the same. General condition somewhat improved. (Yet temp. all the time on the verge of febrile.)

Conclusion for Couple p: The orange case more improved.

Couple q.

31. Or.

Judit Ingeborg Paulina L-v, born $^{25}/_{8}$ 96. Cook. Järfälla.

Anamnesis: Pat. $^{5}/_{9}$. A brother, No. 6, tbc pulm. 1916 at the age of 18. Otherwise no tbc in family. Always well till 1916, then pneumonia ac. sin. Otherwise well till the autumn of 1918, then infl. ep. without complications. Well till April 1922, then infl. Afterwards felt weak without appetite; emaciation, lost 7 kg. last month. Sometimes afebrile temp. No night-sweat. In beginning of May 22 slight hemoptysis. Afterwards sometimes blood-imbibed sputa. Tbc pulm. May 1922.

Admitted $^{4}/_{10}$ 22. *Status* $^{6}/_{10}$: constitution and flesh fairly good. Slight cough with inconsiderable expect. Appetite bad. Feels physically well but is very depressed and cares for nothing. Other organs, no remark.

Local status: right lung, apex scl—II and ssp—A br. ves. resp. and a moderate number of R, hard in scl and submetallic in ssp D 2—D 3 in scl and ssp, D 1—D 2 to II and A. Left lung: D 1—D 2 scl—I and ssp—$^{1}/_{2}$ A, harsh and unclear resp., sparse, fine, hard R.

Extracts from records. $^{17}/_{11}$: right lung anteriorly increased R, scl—III, otherwise as before. Posteriorly distinct R only to 1/2 A. Left lung no R. Coughs hardly ever. Diminished expect. Feels farily well. Sometimes blood-imbibed sputa. Roentgen: indicating pneumothorax? Chiefly right-sided affection with beginning purulence in right apex. $^{7}/_{12}$: peribronchites starting from hilus on both sides, more numerous and closer together on right side, with small consolidations scl—II on the right. $^{30}/_{12}$: right lung anteriorly R scl—II, posteriorly as before. Left lung, no R. Coughs less with rather increased expect. Feels tired, psychially depressed. Since last examination running away during psychosis. No increase in weight. Bacilli: $^{17}/_{10}$ none, $^{2}/_{11}$ +, $^{3}/_{4}$ and $^{20}/_{4}$ none. $^{17}/_{2}$: right lung, R heard only scl—I and ssp—$^{1}/_{2}$ A. Otherwise as before. Coughs occasionally without expect. Still tired. No increase in weight. $^{3}/_{3}$: an orange a day. $^{22}/_{3}$: status idem, but resp. more br. on the right and submetallic R as before. Roentgen shows in the right lung small distinct cavity. Coughs occasionally with inconsiderable expect. Feels fairly well, but continually without increase in weight. $^{7}/_{5}$: local status, isolated R scl—III in right lung, posteriorly to $^{1}/_{2}$ A. Left lung, nothing. Coughs slightly with slight expect. Feels well. Lately some increase in weight. Temp. afebrile. $^{3}/_{6}$ Regained her spirits. Mind changed. No cough.

Weight chart:		Quantity of sputum:	
$^{1}/_{3}$	— 63 kg.	$^{1}/_{3}$	— 10 ccm.
$^{15}/_{3}$	— 63 »	$^{1}/_{4}$	— 10 »
$^{1}/_{4}$	— 63 »	$^{15}/_{4}$	— 10 »
$^{15}/_{4}$	— 61.5 »	$^{1}/_{5}$	— 10 »
$^{1}/_{5}$	— 63 »	$^{15}/_{5}$	— 0 »
$^{15}/_{5}$	— 63.5 »	$^{1}/_{6}$	— 0 »
$^{1}/_{6}$	— 63.8 »	$^{15}/_{6}$	— 0 »
$^{15}/_{6}$	— 63 »		
$^{30}/_{6}$	— 62.5 »		

Summary: A restricted case in Stage III. with half of the right lung affected and with light changes in the left apex. Aggravating at first, cavity formation, psychosis. After starting with the orange experiment locally improved and also general condition considerably better.

32.

Oskar Robert B-n, born $^{2}/_{6}$ 03. Farm labourer. Spånga.

Anamnesis: Pat. $^{3}/_{6}$. Father tbc 3 years ago. Otherwise no tbc in family. As a rule catching cold easily and getting cough. Otherwise always well till the end of Aug.; then fell ill with stabbing pain in his left side. Temp. up to nearly 39° C. Is said to have had pleuritis exsud. sin. in Aug. 22. After that mostly out of bed, but has not been able to work much. Tbc pulm. stated in Sept. 22. Cough and expect. since Aug. 22, bad appetite and emaciation. Never hemoptysis.

Admitted $^{5}/_{3}$. *Status* $^{7}/_{3}$: constitution frail. Flesh spare. Coughs slightly with inconsiderable expect. No breathlessness, appetite fairly good. Feels well. Slight hypertrophy of heart? Systolic accompaniment, strongest

over the apex. Pulm. II acc. Other organs, nothing. *Local status:* left lung all over D 3, upper half resp. of slightly br. character, and hard, partly metallic R; lower half enfeebled resp. and laterally isolated friction sounds. Right lung: scl—II and ssp—A, D 3—D 2 diminishing downwards and br. ves. resp. Anteriorly isolated hard R.

Extracts from records. $^{13}/_{3}$: right lung, no certain R. Left lung, status idem. Hardly ever coughs. Sometimes inconsiderable expect. Feels well. $^{31}/_{3}$: R as on $^{7}/_{3}$. Slight cough with inconsiderable expect. Feels well.

Weight chart:		Quantity of sputum:	
$^{5}/_{3}$	— 52.5 kg.	$^{6}/_{3}$	— 15 ccm.
$^{14}/_{3}$	— 53.5 »	$^{17}/_{3}$	— 10 »
$^{31}/_{3}$	— 56 »	$^{1}/_{4}$	— 10 »
$^{14}/_{4}$	— 57.5 »	$^{1}/_{5}$	— 10 »
$^{1}/_{5}$	— 59 »	$^{15}/_{5}$	— 10 »
$^{15}/_{5}$	— 59.5 »	$^{1}/_{6}$	— 10 »
$^{1}/_{6}$	— 60 »	$^{15}/_{6}$	— 15 »
$^{15}/_{6}$	— 58 »		
$^{30}/_{6}$	— 60 »		

Summary: Case in Stage III. All the left lung with symptoms of cavities in the upper half and pleuritic symptoms in the lower; lighter changes in the apex of right lung. General condition considerably improved. Locally no improvement.

Conclusion for Couple q: Case 32 more extended but less virulent. Case 31 improved more.

Couple r.

33. Or.

Asta Vilfrida K-a, born $^{13}/_{6}$ 16. Labourer's daughter. Solna.

Anamnesis: Maternal grandmother tbc pulm. Parents healthy. During several years relapsing bronchitis. Pertussis at the age of 3. Afterwards weakly. Cough since the summer of 1922, when tbc pulm. was stated, in July. Since then bad appetite, emaciation.

Status on admission $^{27}/_{10}$ 22: general condition exceedingly bad. Pale and thin. Vomited all food. Left lung: D 3 almost everywhere. Tymp. in ssp, below A, and I—III. In these areas br. resp.; amphoric and coarse metallic and grating R. Resp. for the rest unclear, br. ves., numerous hard R. Right lung: $^{1}/_{3}$ A—A some few hard R. Resp. everywhere harsh, not quite clear. Roentgen: all the left lung strong consolidation with three large cavities from base to apex.

Extracts from records. $^{18}/_{11}$: left lung, amphoric resp. nowhere quite pronounced. Anteriorly resp. only softly br. R in toto considerably lessened, less metallic. Right lung, D ssp—beyond $^{1}/_{3}$ A resp. of br. character with isolated hard accompaniments. $^{30}/_{10}$: D as before. Pronouncedly br. resp. only on left side posteriorly, $^{1}/_{3}$ A—A with hard metallic R. For the rest resp. harsh, of slightly br. character with isolated hard accompaniments in some places. Laterally on the left resp. almost extinguished. Right lung as on $^{18}/_{11}$. $^{10}/_{1}$ 23: right lung scl resp. very unclear. Otherwise as on $^{18}/_{11}$. Left lung as on $^{30}/_{11}$. At Christmas cough somewhat increased, especially when moving. Somewhat hoarse. General condition slightly improved. Larynx diffusely reddened. $^{7}/_{2}$: D and resp. as before. R only in right lung I—II and at sp hard without metallic ring, finer. Left lung I—II and ssp—A, some few to several, metallic R, rather coarse, most numerous posteriorly. For

the rest no R. Cough increased of late, trying at the slightest movement. Temp. running higher. General condition improved. Roentgen $^{27}/_{2}$, as before. $^{1}/_{3}$ an orange a day. $^{7}/_{3}$: pneumothorax starting, always standing partial but pressing the cavities together. Expect., up till now abundant, has disappeared. (Narrow lateral pneumothorax, wide adherence in the middle of lung to chest wall, above the clavicle total adherence.) Periodically only slight pneumothorax. $^{19}/_{3}$: anteriorly on the left no resp., no R: posteriorly ssp—A resp. br. with some medium metallic accompaniments. Then resp. feeble, of bronchial character. No certain R. Right lung: II—III and isc resp. br. ves. with suspicion of accompaniment. Cough diminished during last week. Expect. about as before. Pneumothorax continued 50—at highest 100 (generally 80) ccm. under high pressure. At first every other day, in June once a fortnight. $^{18}/_{4}$: left lung anteriorly scl—II resp. feebly audible (pneumothorax partially). For the rest all the way down almost no resp., the same laterally. Posteriorly = $^{19}/_{3}$, but no R. Right lung, no R. Otherwise as before. Cough considerably less with hardly any expect. General condition greatly improved. $^{24}/_{5}$: status quo. Hardly ever coughs. No expect. General condition considerably improved. $^{16}/_{6}$: nowhere R. Resp. in the upper half of left lung br.; then no resp. Right lung: resp. everywhere harsh. Otherwise no remark. General condition improved. Temp. some time afebrile, mostly febrile with high points, especially after insufflations, yet less after March. At the end temp. a — subfebrile (like that of the others).

Weight chart:

$^{26}/_{10}$ — 17 kg.	$^{15}/_{1}$ — 18.7 kg.	$^{15}/_{4}$ — 19.5 kg.
$^{31}/_{10}$ — 17 »	$^{1}/_{2}$ — 19.3 »	$^{1}/_{5}$ — 19.5 »
$^{15}/_{11}$ — 17 »	$^{15}/_{2}$ — 19.5 »	$^{15}/_{5}$ — 20 »
$^{1}/_{12}$ — 18,5 »	$^{15}/_{3}$ — 18.5 »	$^{1}/_{6}$ — 20.5 »
$^{15}/_{12}$ — 18,7 »	$^{1}/_{4}$ — 18.5 »	$^{15}/_{6}$ — 20 »
$^{1}/_{1}$ — 18.7 »		

Summary: Case in Stage III., left lung totally attacked with large cavities. Right lung, hilus process with peribronchites. Favourably influenced by pneumothorax treatment (sputa disappeared). General condition greatly improved. Improvement in general condition is regarded as surpassing what might have been expected as a consequence of and during the pneumothorax treatment.

34.

Ernst Napoleon L-n, born $^{17}/_{11}$ 97. Täby.

Anamnesis: Pat. $^{3}/_{3}$. (One brother suspected for tbc pulm.) Fell ill with fever and stabbing pain in the left side $^{11}/_{12}$ 1922. In bed two weeks with fever. Then cough and expect since Jan. 1923. Never hemoptysis. Advised hospital nursing by physician Febr. 1922. Admitted to the Väsby Hospital $^{22}/_{3}$ 23. Removed to the tbc department $^{31}/_{3}$ 23 as tbc pulm. and pleurit. exsud. sin. were stated. Appetite since beginning of the year bad. Emaciation.

Extracts from records. $^{5}/_{4}$: right lung scl—II and ssp—$^{1}/_{2}$ A, D 3—D 2 with enlarged unclear resp. No R. Below no D, but resp. harsh, isolated R. Left lung below II and $^{1}/_{2}$ A D 3 with hardly audible resp., and feeble br. resp. at the bottom. Some few submetallic R, intermingled with friction sounds. Other organs, nothing. $^{19}/_{5}$: appetite good as before. D and resp. the same. R are only heard in left lung about A and in right lung at the top in the axilla. Hardly ever coughs. Practically no expect. Feels well. Temp. afebrile.

Tests for bacilli in the hospital $^{26}/_{3}$ positive; in the tbc department on $^{3}/_{4}$, $^{10}/_{4}$ and $^{20}/_{4}$: No bacilli.

Weight chart:

$^{31}/_{3}$ — 63.5 kg.
$^{14}/_{4}$ — 66.5 »
$^{1}/_{5}$ — 68.5 »
$^{15}/_{5}$ — 68.5 »
$^{1}/_{6}$ — 69.5 »
$^{15}/_{6}$ — 71.5 »
$^{30}/_{6}$ — 71 »

Quantity of sputum:

$^{1}/_{4}$ — 5 ccm.
$^{1}/_{5}$ — 0 »
$^{15}/_{5}$ — 15 »
$^{1}/_{6}$ — 10 »
$^{15}/_{6}$ — 10 »

Summary: Case in Stage III. with light affection of right apex and graver of the lower half of left lung. Locally and generally considerably improved.

Conclusion for Couple r: Similar progress.

Couple s.

35. Or.

Karin Elisabet J-n, born $^{9}/_{3}$ 1913. Labourer's daughter.

Anamnesis: Nursed here since $^{5}/_{12}$ 1917 to $^{30}/_{3}$ 1918 for bronchitis and in the tbc department. Since then periodically weakly, has not been able to go to school. Occasionally rising temp. Last days fever to 40° C.

Admitted $^{5}/_{12}$. Pale, thin, feeble. *Status* $^{6}/_{12}$: right lung, isc D 1—D 2, harsh, unclear resp. No certain R. Left lung: parasternal D 1; D 2—D 3 I—II. No certain R. Roentgen examination $^{5}/_{12}$; enlarged hilus with peribronchites on both sides, most on the right.

Extracts from records. $^{10}/_{1}$: lungs status quo. $^{7}/_{2}$: right laterally II—IV isolated accompaniments. Never coughs. Poor increase in weight. $^{2}/_{3}$: an orange a day. $^{7}/_{3}$ D and resp. = $^{6}/_{12}$. No certain accompaniments. Tonsillotomy bilat., healed $^{19}/_{2}$. $^{18}/_{4}$: laterally on the left, suspicion of accompaniments. For the rest no R. Resp. and D as before. Never coughs. General condition as before. $^{24}/_{5}$: nowhere R or accompaniments. Never coughs. General condition considerably improved. $^{15}/_{6}$: status idem. General condition still more improved. Getting stout, temp. subfebrile with points. Appetite began to grow a little better at Christmas-time. Distinct improvement from the middle of March.

Weight chart:

$^{5}/_{12}$ — 27.5 kg.
$^{15}/_{12}$ — 27.5 »
$^{1}/_{1}$ — 28.2 »
$^{15}/_{1}$ — 28.6 »
$^{1}/_{2}$ — 28.5 »
$^{15}/_{2}$ — 28.3 kg.
$^{1}/_{3}$ — 29 »
$^{15}/_{3}$ — 30 »
$^{1}/_{4}$ — 31 »
$^{15}/_{4}$ — 31 »
$^{1}/_{5}$ — 31.5 kg.
$^{15}/_{5}$ — 32.3 »
$^{1}/_{6}$ — 33 »
$^{15}/_{6}$ — 32.8 »

Summary: Case in Stage I. of hilus tbc without certain R. Considerably improved general condition.

36.

Irma Kristina L-m, born $^{24}/_{9}$ 1911. Mason's daughter. Solna.

Anamnesis: Mother tbc pulm. 5-para. Nursed here for 4 months 1921. Since then, according to dispensary, process at standstill. Pat. born 6 weeks too early. Always weak and frail. Disposition for colds and sore throat. Began coughing about a year ago. Tbc pulm. stated in summer 1922.

Admitted $^{16}/_{1}$ 23. *Status:* Pale, thin, weakly, exceedingly bad appetite. *Lung status:* right lung D 1—D 2, sc—III and ssp—A and in a small area around A on the left. Right lung I—II and interscap. slightly br., as also in left isc. For the rest harsh and unclear resp. Isolated — some few fine R in the right isc and in the indicated area posteriorly on the left. Roentgen: bilateral enlargement of the hilus shadow, more on the right. Shadow on the left apex. $^{7}/_{2}$: right lung posteriorly ssp—A resp. less pronouncedly bronchial. For the rest, idem. $^{7}/_{3}$: never coughs; general condition as before. Left lung very harsh resp. $^{1}/_{2}$ A—downwards. Right lung unclear resp. No R. Somewhat shorter tone in isc, but less pronounced than before. $^{15}/_{4}$: right lung isc resp. harsh, unclear. At the base posteriorly and laterally, isolated fairly loose R. For the rest nothing. Left lung: $^{1}/_{2}$ A—A isolated inconsiderable dry accompaniments. For the rest as before. $^{24}/_{5}$: nowhere certain accompaniments (suspicion of such around A on the left). Never coughs. General condition improved. $^{16}/_{6}$: left lung around A sometimes isolated accompaniments. Right isc at deep resp. br. character. General condition as before. Never coughs. Feels well. Temp. sometimes subfebrile (points, like Case 35). Appetite not so good, until last month. $^{4}/_{6}$: like the other children moved into new premises.

Summary: Case of hilus tbc with R in right isc and around left ang., which on the whole have disappeared. For the rest, locally idem. General improvement less than the parallel case.

Weight chart:

$^{16}/_{1}$ — 30 kg.	$^{15}/_{3}$ — 31 kg.	$^{15}/_{5}$ — 32 kg.
$^{1}/_{2}$ — 30 »	$^{1}/_{4}$ — 31.3 »	$^{1}/_{6}$ — 32.5 »
$^{15}/_{2}$ — 30 »	$^{15}/_{4}$ — 31.5 »	$^{15}/_{6}$ — 32 »
$^{1}/_{3}$ — 31 »	$^{1}/_{5}$ — 32 »	

Conclusion for Couple s: Greater improvement for the orange case.

Couple t.

37. Or.

Ivar M-n, born $^{24}/_{8}$ 1915. Labourer's son. Huvudsta.

Anamnesis. Mother suffering from chest affliction, a maternal aunt nursed in sanatorium. Pat. twin. Had pertussis as an infant. Three years ago severe lung catarrh. Always weak and easily catching cold. Last year breathlessness, easily perspiring, even at night. Was to begin school in the autumn 1922, at examination hypertrophy of hilus. Advised hospital treatment. Temp. subfebrile all through the autumn and winter.

Admitted. $^{16}/_{1}$ 23. *Status:* appetite indifferent. *Local status:* both lungs anteriorly scl—II, D 1—D 2; posteriorly right lung, ssp—$^{1}/_{3}$ A and a small area around A, D 1. D to the fifth dorsal vertebra. No R. Resp. harsh, enfeebled, unclear diffusely over both lungs. Both isc, suspicion of accompaniments. Roentgen $^{16}/_{1}$: considerably enlarged hilus shadows on both sides.

Extracts from records. $^{7}/_{4}$ signs of diffuse bronchitis, more in the left lung. Otherwise as before. $^{2}/_{5}$: an orange a day. $^{19}/_{5}$: bronchitis better. Otherwise as before. General condition better. $^{15}/_{4}$: both isc D with resp. unclear. For the rest nothing. Never coughs. Temp. still subfebrile. General condition as before. Dismissed $^{22}/_{4}$ 23.

Weight chart:

$^{16}/_{1}$ — 26.5 kg.	$^{1}/_{3}$ — 27 kg.	$^{1}/_{4}$ — 27.9 kg.
$^{1}/_{2}$ — 26.5 »	$^{15}/_{3}$ — 27.5 »	$^{15}/_{4}$ — 27.8 »
$^{15}/_{2}$ — 26.5 »		

Summary: Bilateral hilus-gland tbc with peribronchites, without certain R. General condition somewhat improved already before starting the orange cure; after that considerable improvement of general condition and marked improvement of lung status.

38.

Ingrid Linnea K-n, born $^{9}/_{10}$, 1911. Labourer's daughter. Hagalund.

Anamnes. Pat. $^{1}/_{3}$. No tbc in family. Morbilli, pertussis at the age of $2^{1}/_{2}$. At the age of 3 peritonitis. Since then weakly and thin. Easily catching cold. In the beginning of Dec. 1922 she fell into the water, after that cough and fever. Nursed in the Allmänna Barnhuset $^{7}/_{12}$ 22—$^{24}/_{2}$ 23 for tbc pulm. (Roentgen).

Admitted $^{24}/_{2}$ 23. Roentgen: both hilus greatly enlarged with peribronchites downwards. *Status* $^{7}/_{3}$: left lung isc short tone and dry R all the way down. Right lung: isc somewhat short tone and buzzing resp. with accompaniments. Rather pale and thin. Appetite fairly good.

Extracts from records. $^{18}/_{4}$: left lung I—II and isc. isolated dry accompaniments. For the rest nothing. Right lung, everywhere unclear resp., but no accompaniments. Still coughs a great deal. General condition improved. $^{24}/_{5}$: right lung, around mamill. isolated dry accompaniments. Left lung: $^{1}/_{2}$ A—downwards in places isolated — some few dry R. Otherwise nothing. Coughs less. Generally improved. $^{15}/_{6}$: lung status idem.

Temp. generally subfebrile, sometimes a little above 38° C.

Weight chart:

$^{27}/_{2}$ — 27 kg.	$^{1}/_{4}$ — 27.4 kg.	$^{15}/_{5}$ — 29 kg.
$^{1}/_{3}$ — 26 »	$^{15}/_{4}$ — 28 »	$^{1}/_{6}$ — 29.5 »
$^{15}/_{3}$ — 26.5 »	$^{1}/_{5}$ — 28.3 »	$^{15}/_{6}$ — 29.5 »

Summary: Bilateral hilus tbc with peribronchites. Generally improved, locally sooner aggravated, like the cough. Less improved than might have been expected.

Conclusion for Couple t: Greater improvement of the orange case.

Couple u.

39. Or.

Carl Evert L-n, born $^{3}/_{3}$ 1919. Farmer's son. Össebygarn.

Admitted $^{1}/_{3}$ 23. Has tbc genu sin.; a year ago nursed in the Väsby Hospital. Capsular changes with small effusion (nothing in the bone). *Local status* $^{1}/_{3}$: both isc, more on the right, resp. very harsh, not quite clear. Isolated rhoncus in right isc. Otherwise nothing. Roentgen $^{3}/_{3}$: bilaterally enlarged hilus, more on the right.

Extracts from records. $^{2}/_{3}$: an orange a day. $^{7}/_{3}$: right isc resp. harsh. Otherwise nothing. $^{18}/_{4}$: sometimes in both isc isolated creaking accompaniments. Never coughs. General condition considerably improved. $^{24}/_{5}$: status idem. General condition improved. $^{29}/_{6}$: resp. still harsh in both isc. Otherwise nothing. Never coughs. General condition greatly improved.

Weight chart:

$^{1}/_{3}$ — 16.5 kg.	$^{1}/_{3}$ — 17.5 kg.	$^{1}/_{4}$ — 18.2 kg.
$^{15}/_{3}$ — 16.5 »	$^{15}/_{3}$ — 17.9 »	$^{15}/_{6}$ — 18.7 »

Not weighed during the time $^{1}/_{4}$—$^{15}/_{6}$ on account of a large plaster-bandage.

Summary: Bilateral hilus-gland tbc, more in right lung, with complications in left knee. Local symptoms unchanged. General condition improving the whole time. Appetite good all through.

40.

Carl Thore Lennart J-n, born $^{14}/_{9}$ 1919, Labourer's son. Solna.

Anamnesis: Pat. $^{1}/_{1}$. Father tbc in 1921, now well. Pat. always weakly, pale, easily catching cold. Bad appetite. $^{3}/_{1}$ 23: Pirquet pos.

Admitted $^{8}/_{1}$ 23. *Status:* Left side, both isc short tone, resp. very harsh, unclear. Suspicion of accompaniments. Temp. mostly subfebrile with isolated higher points.

Extracts from records. $^{7}/_{2}$: bronchitic symptoms. Rhonchi over both lungs. Right lung below A and laterally to the left half-hard accompaniments. Left lung in toto shorter tone. Last days increased cough. General condition improved. $^{7}/_{3}$: left lung, shorter tone nearly over the whole lung, increasing downwards. Resp. harsh. Right lung, resp. harsh, especially in isc. Now no accompaniments.

Roentgen $^{19}/_{4}$: enlarged hilus fields on both sides. $^{29}/_{4}$: scraping at the back of nose. Dismissed $^{30}/_{5}$ 23.

Weight chart:

$^{8}/_{1}$ — 15.2 kg.	$^{15}/_{2}$ — 17.2 kg.	$^{15}/_{3}$ — 17.8 kg.
$^{15}/_{1}$ — 15.5 »	$^{1}/_{3}$ — 17.8 »	$^{30}/_{3}$ — 18.2 »
$^{1}/_{2}$ — 16.5 »		

Summary: Bilateral hilus-gland tbc. General condition improved. Possibly also some local improvement.

Conclusion for Couple u: Similar improvement.

Couple v.

41. Or.

Evald Torgny V-n, born $^{8}/_{8}$ 19. Carters' son. Lövö.

Anamnesis: No tbc in family. Well till last spring, then began growing thin and getting delicate. Pertussis at midsummer, afterwards bad general condition. Cough considerably lessened.

Admitted $^{8}/_{8}$ 22. *Status:* general condition bad, appetite bad. *Local status:* upper half of left lung short tone. Lower half softened tympanism, specially distinct below A. Resp. everywhere very harsh, isc almost bronchial. Diffusely over the whole lung rhonchi and hard, almost creaking R. Right lung: nowhere quit clear lung tone, resp. everywhere harsh, not quite clear. In some places isolated rhonchi and R (partly from elsewhere?).

Extracts from records. $^{5}/_{11}$: changes in right lung possibly increased. General condition improved. $^{1}/_{11}$: only below A on both sides isolated mostly dry accompaniments. For the rest no accompaniments or R. $^{3}/_{11}$: Roentgen. Left lung, distinct shadow from hilus upwards, also a little downwards. Right lung, distinct enlargement of hilus. $^{24}/_{11}$: rhonchi and R as on admission diffusely over both lungs. $^{8}/_{12}$: diffusely over both lungs rather coarse R, especially posteriorly below A bilaterally. Short tone on the right laterally and in isc. $^{10}/_{1}$ 23: left lung, numerous dry coarse R over the whole lung, mostly over the base. Right lung, isolated rhonchi diffusely over the whole lung. Resp. and D everywhere as before. Still coughing as before. General condition improved. $^{7}/_{2}$: D 1 all over the right lung, D 2 over the left, stronger posteriorly. Resp. as before. Rhonchi diffusely over both. Still fits of cough-

ing, but considerably less than before. General condition improved. Roentgen 21/2: enlarged hilus shadows with peribronchites, mostly in left lung downwards. Appearance suggests tbc. 2/3: an orange a day. 19/3: right lung below III, isolated — some few fairly hard accompaniments. For the rest no R or accompaniments. D and resp. as before. Last week bad appetite. General condition as before. 15/4: right lung accompaniments as before. Left lung below A isolated rhonchi. For the rest no R or accompaniments. Hardly ever coughs. General condition improved. 24/5: nowhere R. For the rest as on 7/3. Never coughs. 16/6: resp. everywhere very harsh. D inconsiderable in left scl and base. Right lung no D or R, but harsh resp. Nowhere R. Coughs hardly ever. Dismissed 22/6.

Summary: Bilateral hilus tbc with diffusely spread peribronchites. Before giving the orange general condition improved, but no local improvement. After the orange considerable improvement of local status and also of general condition, specially of appetite (flesh and weight were good when the orange was first given). Greater improvement than might have been expected.

Weight chart:

8/9 — 13 kg.	15/12 — 15.5 kg.	1/4 — 16.7 kg.
15/9 — 14.3 »	1/1 — 16.5 »	15/4 — 17.3 »
1/10 — 15.3 »	15/1 — 16.5 »	1/5 — 17.3 »
15/10 — 15.3 »	1/2 — 16.5 »	15/5 — 17.3 »
1/11 — 16.2 »	15/2 — 17.5 »	1/6 — 17.3 »
15/11 — 16.2 »	1/3 — 17.5 »	15/6 — 17 »
1/12 — 15.5 »	15/3 — 17.5 »	

Couple w.

43. Or.

Gustaf Ruben T-n, born 3/1 11. Carter's son. Hagalund.

Anamnesis: No tbc in family. Always been weak and thin. Has had morbilli, pertussis and pneumonia when three years old. Bronchial catarrh every year since two years old. Is said to have had attacks of asthma every year since he was 7. During the last years more frequent attacks. Admitted 16/2. Bad appetite, thin. Both isc and I—III D 2. Besides, D 1—D 2 in right lung below A. Resp. in both isc of br. character with isolated inconstant mostly dry accompaniments. Right lung below A and anteriorly laterally isolated fairly coarse dry R. Resp. for the rest in both lungs harsh, unclear. No constant accompaniments. Roentgen 16/2: both hilus considerably enlarged, the right more, with consolidation towards the base.

Extracts from records. 2/3: an orange a day. 9/3: R only right isc, D and resp. as before. Never coughs. 1/4: D as before. No R. Resp. harsh, br. ves. as before. No cough. Dismissed 25/4 = 1/4. Appetite considerably improved after orange; general condition also. Breathlessness gone.

Weight chart:

16/2 — 25.3 kg.	15/3 — 27.5 kg.	15/4 — 29 kg.
1/3 — 25.7 »	1/4 — 29 »	

Summary: Bilateral hilus affection with slight consolidation in base of right lung. Both locally and generally improved after the orange.

44.

Inga Maj Elisabet P-t, 4 years old.

Nursed in the Allmänna Barnhuset for pertussis + pneum. ac. dx. + tbc lphgl. bronch. June—Aug. 1922. Apparently well in the middle of Aug.

Afterwards nursed in the Serafimerlasarettet till admitted into the Sanatorium $^{21}/_{10}$ 22.

Status $^{21}/_{10}$: right lung, lower half D with tymp. accompaniments and unclear respiration verging on br. ves. Uncertain accompaniments. Left lung below A, D + resp. harsh. Inconstant accompaniments in some places laterally. $^{3}/_{11}$ Roentgen: enlarged hilus shadows on both sides, most on the right. Shadow of the left base. $^{30}/_{11}$: Left lung, laterally fairly certain fine accompaniments. For the rest status quo. $^{10}/_{1}$ 23: right lung $^{1}/_{2}$ A—A isolated accompaniments. Left lung: isolated rather dry accompaniments laterally. For the rest as before. Coughs slightly at times. General condition improved. $^{7}/_{2}$: right lung, nowhere certain accompaniments. Left lung, below A and laterally some slight coarse accompaniments. Otherwise as before. Hardly ever coughs. General condition improved. $^{19}/_{4}$: right lung below A sometimes suspicion of dry accompaniments. Left lung: no certain accompaniments. General condition as before. Last week bad appetite. $^{18}/_{4}$: right lung I—III and isc resp. unclear, harsh, of almost br. character. On the right laterally resp. enfeebled. Nowhere certain accompaniments. Never coughs. No expect. Appetite better. General condition as before. $^{24}/_{5}$: Nowhere R or accompaniments. For the rest status quo. Bad appetite. Never coughs.

Weight chart:

$^{15}/_{2}$ — 15.5 kg.	$^{15}/_{4}$ — 15.4 kg.	$^{1}/_{6}$ — 15 kg.
$^{1}/_{3}$ — 16 »	$^{1}/_{5}$ — 15 »	$^{15}/_{6}$ — 15.5 »
$^{15}/_{3}$ — 15 »	$^{15}/_{5}$ — 15.3 »	$^{1}/_{7}$ — 15.5 »
$^{1}/_{4}$ — 15.3 »		

Summary: Bilateral hilus tbc, most on right side. Before $^{1}/_{3}$ improved, afterwards aggravation with regard to general condition (appetite!) and also locally.

Conclusion for Couple w: The orange case has improved more.

Literature cited.

ABDERHALDEN, E., and WERTHEIMER, E.: Weitere Beiträge zur Kenntniss von organischen Nahrungsmitteln mit spezifischer Wirkung. Pflügers Archiv f. Physiol., 191, 1921, p. 258.

ABELS, H.: Über die Rolle der Infekte beim Skorbut der Kinder und Säuglinge. Med. Klin. No. 43, 1919, p. 1084.

ADAMS, J., and HAMILTON, A.: A visit to Germany. Brit. Journ. Childr. Dis. July-Sept., 1919, p. 127.

ANDERSON, E. V., DUTCHER, R. A., ECKLES, C. H., and WILBUR, J. W.: The influence of heat and oxidation upon the nutritive and antiscorbutic properties of cow's milk. Science, N. S., Vol. 53, No. 1375, p. 446.

——: The nutritive and antiscorbutic properties of milk. Journ. Biol. Chem. 45, 1920.

ARON, H.: Ansatzfördernde Wirkung von Extraktstoffen. Mon. Kh., Bd. 22, 1921—1922.

ASCHOFF, L., and KOCH, W.: Skorbut. Jena 1919.

BAGINSKY, A.: Möller-Barlowsche Krankheit. Eulenburgs Realenzyklopädie, 4. Aufl.

BAHRDT, H., and EDELSTEIN, F.: Organanalysen bei Barlow'scher Krankheit. Z. f. Kh., Bd. 9, 1913, p. 415.

BARDIN, M:me: Scorbut infantile. Thèse de Paris. 1903.

BARLOW, TH.: On cases described as acute rickets. Med. Chir. Transact. 66, 1883, p. 159.

——: Cyclopaedia of the diseases of children. Keating. Vol. II, 1889, p. 265.

——: Der infantile Scorbut. Cbl. f. inn. Med., Bd. 16, 1891, p. 505.

——: Traité des maladies de l'enfance. Grancher. II, 1897, p. 173.

BARNES, R. E., and HUME, E. MARG.: Comparison between the antiscorbutic properties of fresh, heated and dry cow's milk. Lancet, 1919, p. 323.

BARTENSTEIN, L.: Beiträge zur Frage des künstlichen Morbus Barlow bei Tieren. Jahrb. f. Kh., Bd. 61, 1905, p. 6.

BAUMANN, L., and HOWARD, C. P.: Metabolism of scurvy in an adult. Arch. Int. Med., 9, 1912, p. 665.

——: The mineral metabolism of experimental scurvy of the guinea-pig. Am. Journ. Med. Sci., 103, 1917, p. 650.

BEDSON, PH.: Brit. Med. Journ., II, 1921, p. 792.

BEITZKE, H.: Fortschreitende Phtisen. Handb. d. ärztl. Erf. im Weltkriege, Bd. 8, p. 63.

BERG, R.: Die Vitamine. Leipzig 1922.

BEZSSONOFF, V.: Préparation antiscorbutique. Bull. d'hyg. alimentaire, No. 1, 1923, p. 14.

BIERICH, R.: Über Scorbut. D. Arch. f. klin. Med., 1919, p. 151.
BOLLE: Zur Therapie der Barlowscher Krankheit. Z. f. diät. u. physik. Therapie, Bd. 6, 1903.
BRANDT, H.: Blutuntersuchungen bei Barlowscher Krankheit. D. m. W., Bd. 45, 1919, p. 646.
CARRELL, A.: Cicatrization of wounds. Journ. Exp. Med., 34, 1921, p. 425.
CHICK, H., and DALYELL, E.: Eine Scorbutepidemie unter Kindern im Alter von 6 bis 14 Jahren. Z. f. Kh., 26, 1920, p. 257.
CHICK, H., and HUME, E. M.: Note on the importance of accurate and quantitative measurements in experimental work on nutrition and accessory food factors. Journ. Biol. Chem., 39, 1919, p, 203.
CHICK, H., HUME, E. M., and SKELTON, R. F.: Antiscorbutic value of cow's milk. Biochem. Journ., Bd. 13, p. 137.
COHEN, B., and MENDEL, L. B.: Scurvy in relation to diet. Journ. Biol. Chem., 35, 1918, p. 425.
CORDIER: Discussion after Mouriquand, Lyon Méd. 1922.
CORNET, G., and KOSSEL, H.: Tuberkulose. In Kolle-Wassermann: Hb. d. path. Mikroorganismen, Bd. 5, 1913.
CRAMER, W., and MOTTRAM, J. C.: Similarity of effects, produced by absence of vitamines and by exposure to X-rays and radium. Lancet 1921, p. 963.
DARLING, S. T.: Pathological affinities of beri-beri and scurvy. Journ. Am. Med. Ass., 62, 1914, p. 1290.
DAVEY, A. J.: Determination of the minimum protective doses. Biochem. Journ., Bd. 15, 1921, p. 83.
DELF, E. M.: Effect of heat on the antiscorbutic factor. Biochem. Journ., Bd. 14, 1920, p. 227.
DELF, E. M., and SKELTON, R. F.: Effect of drying on the anti-scorbutic. Biochem. Journ., Bd. 12, 1918, p. 448.
DELF, E. M., and TOZER, F. M.: The antiscorbutic value of cabbage. Biochem. Journ., Bd. 12, 1918, p. 416.
——: On the histological diagnosis of experimental scurvy. Ibid., p. 445.
DRUMMOND: Some aspects of infant feeding. Lancet 1918, II, p. 482.
DRUMMOND, C. J., Note on the rôle of the antiscorbultic factor in nutrition. Biochem. Jl. 13, 1919, p. 77.
DUTCHER, R., ECKLES, A., DAHLE, C. H., MEAD, S. W., SHAEFER, O. G.: Vitamine studies IV. Journ. Biol. Chem., 45, 1920—21.
DUTCHER, R., HERSHAW and HALL: Vitamine studies VIII. Journ. Biol. Chem., 1921, 47, p. 483.

ELLIS, N. R., STEENBOCK, H., and HART, E. B.: Some observations on the stability of the antiscorbutic vitamine. Journ. Biol. Chem., 46, 1921, p. 367.

EPSTEIN, A.: Über eine auffällige Häufung der Barlowscher Krankheit in den Kriegsjahren 1917—1918. Jb. f. Kh., 88, 1918, p. 237.

ERDHEIM, Über das Barlowherz. W. kl. W., No. 49, 1918, p. 1293.

FABER: A study of the antiscorbutic value of honey. Journ. Biol. Chem., 43, 1920, p. 113.

FINDLAY, G. M.: The blood and blood-vessels in guinea-pig scurvy. Journ. Path. and Bact., Bd. 24, 1921, p. 446.

——: The effects of an unbalanced diet in the production of guinea-pig scurvy. Biochem. Journ., 15, 1921, p. 355.

FINDLAY, G. M., and MACKENZIE, R.: Biochem. Jl. 16, 1922, p. 574.

FINKELSTEIN: Säuglingskrankheiten. 1921, p. 349.

——: D. M. W., No. 38, 1920, p. 1063.

FRAENKEL, E., Fortschritte a. d. Geb. d. Röntgenstr., 7, 1903—04. 10, 1906—07.

——: Die Möller-Barlowsche Krankheit. Ibid. Erg. Bd. 18, 1908.

FRANK, H.: Stoffwechsel in der Möller-Barlowschen Krankheit. Z. f. Kh., 27, 1921.

FRANK, M.: Jhrb. f. Kh., Bd. 91, 1920, p. 21.

FREISE: Experimentelle Untersuchungen über die Ernährungsbedingungen des Wachsthums. Jhrb. Kh., Bd. 91, 1920, p. 79.

FREUNDENBERG, E.: Antiscorbutische und oxydationsfördernde Wirkungen der Extraktstoffe. Mo. Khk., Bd. 22, 1921—22, p. 370.

FREUNDENBERG, E., and GYÖRGY, P.: Münch. Med. Woch. 67, 1920, 1061.

FRÖLICH, THEODOR: Experimentelle Untersuchungen über den infantilen Scorbut. Z. Hyg., 72, 1912, p. 155.

FÜRST, VALDEMAR: Weitere Beiträge zur Ätiologie des experimentellen Scorbuts des Meerschweinchens. Z. Hyg., 72, 1912, p. 121.

FUNK, CASIMIR: The vitamins. Baltimore 1922.

GEOGHEGAN, J.: Tuberculosis from a West Indian standpoint. Lancet 1919, p. 56.

GERHARTZ, H.: Einfluss des Ernährungszustandes, des Alters und anderer allgemeinen Umstände auf den Verlauf der Tuberkulose. Brauers Beitr. z. Klin. d. Tuberk., Bd. 53, H. 2/3, Nov. 1922.

GERSTENBERGER, H. J.: Amer. Journ. Med. Sci., 155, 1918, p. 253.

GIVENS, M., and MCCLUGGAGE, H. B.: Antiscorbutic property of vegetables. I. Journ. Biol. Chem., 37, 1919, p. 253.

GIVENS, M. and MCCLUGGAGE, H. B.: The effect of heat and age upon the antiscorbutic vitamine in tomatoes. Proc. Soc. Exp. Biol. and Med., Vol. 18, No. 5, 1921, p. 164.

GIVENS, M. H., MCCLUGGAGE, H. B., and v. HORNE: The antiscorbutic property of apples and bananas. Proc. Soc. Exp. Biol. and Med., Vol. 18, 1921, p. 140.

GODLEVSKI: Carence partielle et préscorbut. Presse médicale, No. 69, 1921, p. 682.

GRÜNER, O., and HAMBURGER, F.: Experimentelle Untersuchungen über die Tuberkuloseinfektion. Beitr. z. Klin. d. Tuberk., 17, 1910, p. 1.

GYÖRGY, P.: Jhb. d. Khk., 94, 1921, p. 55.

HAPP, W., and WAGNER, R.: Z. Kkh. 35, 1923, p. 125.

HARDEN, A., and ZILVA, S. S.: Antiscorbutic requirement of the monkey. Biochem. Journ., 14, 1920, p. 131.

HART, C.: Die Herzmuskelverkalkung. Frankf. Z. f. Path., III: 3, 1909.

——: Infantiler Scorbut. Jhb. f. Kh., 76, 1912, p. 507.

HART, C., and LESSING, O.: Der Scorbut der kleinen Kinder. Stuttgart 1913.

HART, E. B., STEENBOCK, H., ELLIS, N. R.: Antiscorbutic potency of milk-powders. Journ. Biol. Chem., 46, 1921.

HAUSSMANN, TH. P.: Das Blutbild bei Scorbut. Z. f. klin. Med., Bd. 93, H. 4/6, 1922, p. 346.

HAWK, P. B., SMITH, C. A., BERGHEIM, O.: Vitamin content of honey. Am. Journ. Physiol., 55, 1921, p. 339.

HAYEM, M. G.: Note sur l'anatomie pathologique de Scorbut. Gaz. méd., No. 13, 1871, p. 126.

HÉRICOURT et RICHET, C.: Zomothérapie. C. rend. Acad. Sciences, 130, 1900, p. 605.

HERXHEIMER, GOTTHOLD: Grundlagen der pathologischen Anatomie. München 1922.

HERZOG, F.: Über experimentellen Scorbut bei Meerschweinchen. Frankf. Z. f. Path., Bd. 26, 1921—22.

HESS, ALFRED: Jl. Am. Med. Ass. 65, 1915, p. 1003.

——: Infantile scurvy III. Journ. Dis. Childr., 13, 1916, p. 152.

——: Jl. biol. Chem. 35, 1918, p. 487.

——: Scurvy — Past and Present. Philadelphia 1920.

——: Newer aspects of some nutritional disorders. Journ. Am. Med. Ass., 76, 1921, p. 693.

HESS, ALFRED, and UNGER, LESTER: The destructive effect of oxidation on antiscorbutic vitamin. Proc. Soc. Exp. Biol. and Med., Vol. 18, No. 5, 1921, p. 143.

——: Scorbutic beading of the ribs. Am. Journ. Dis. Childr., No. 5, 1920, p. 331.

——: The scurvy of guinea-pigs. Journ. Biol. Chem., 35, 1918, pp. 479, 487.
——: Scurvy of guinea-pigs. III. Journ. Biol. Chem., 38, 1919, p. 293.
Hess, Alfred, Unger, Lester, and Supplee, G. C.: Relation of fodder to the antiscorbutic potency of milk. Journ. Biol. Chem., 45, 1920, p. 229.
Heubner, O.: Über die Barlowsche Krankheit. B. kl. W., 1903, p. 285.
Hoffmann, W.: Untersuchung eines Falles von Barlowscher Krankheit. Zieglers Beitr., Suppl. 7, 1905, p. 702.
Holmgren, E.: Histologi. Stockholm 1920.
Holst, Axel: Shipberiberi and scurvy. Journ. Hyg., 7, 1907, p. 619.
Holst, Axel, and Frölich, Theodor: Ship-beriberi and scurvy. Journ. Hyg., 7, p. 634.
——: Über experimentellen Scorbut. Z. Hyg., Bd. 72, 1912, p. 1.
——: Über experimentellen Scorbut. Z. Hyg., Bd. 75, 1913, p. 334.
——: Fortsatte undersøkelser om skørbuk etc. N. Mag. f. Lv., 1916, p. 1009.
Hopkins, Gowland: On the present position of vitamins in clinical medicine; with discussion. Br. Med. Journ., 1920, p. 147.
——: Lancet 200, 1921, p. 1.
Howard, C. P., and Ingvaldsen, T.: The mineral metabolism of experimental scurvy of the monkey. Johns Hopkins Hosp. Bull., 28, 1917, p. 222.
Howe, P. R.: Effects of scorbutic diets upon the teeth. Dental Cosmos, Bd. 62, 1920, p. 586.
——: Dental caries. Ibid., p. 921.
——: The effect of vitamin deficient diet upon the teeth. Dental Cosmos, 1921, p. 1086.
——: Effect of diet upon the teeth and bones. Journ. Am. Dent. Ass., No. 3, 1923, p. 201.
——: Food accessory factors in relation to teeth. Journ. Dent. Research, March 1921.
Höjer, A., Fall av levercirrhos. Hygiæa 1919, p. 955.
——: Översikt av vitaminforskningarna. Hygiæa 1920, p. 449.
Ide, T.: Gefässveränderungen bei der Möller-Barlowschen Krankheit. Z. f. Khk., 32, 1922, p. 165.
Ingier, Alexandra: Beiträge zur Kenntniss der Barlowschen Krankheit. Frankfurt. Ztschr. f. Path., 14: 1, 1913.
——: A study on Barlow's disease, experimentally produced in fetal and newborn guinea-pigs. Journ. Exp. Med., 21, 1915, p. 525.
Iwabuchi, T.: Über Nebennierenveränderungen bei experimentellem Scorbut. Beitr. z. Path. Anat., Bd. 70, 1922, p. 440.

IWABUCHI, J.: Über Organanalysen bei experimentellem Scorbut. Z. f. d. ges. exp. Med. 30, 1922, p. 76.

JACKSON, L., and MOORE, J. J.: Studies on experimental scurvy in guinea-pigs. Journ. Inf. Dis., 19, 1916, p. 511.

JACOBSTHAL, H.: Zur Pathologie der Knochenerkrankungen bei Barlowscher Krankheit. Beitr. z. Path. Anat. XXVII, 1900, p. 173.

JANSEN, W. H.: Die Ödemkrankheit. D. Arch. f. klin. Med., Bd. 131, 1919—20, p. 144.

JOEST, E., und EMMHOFF, E.: Studien über die Histogenese der Lymphdrüsentuberkels. Virschows Arch., 210, 1912, p. 188.

JOSIAS: Traitement de la tuberculose pulmonaire chez les enfants par le suc musculaire et la viande crue. Revue d'hygiène et de médec. infant., No. 1. 1902.

JOSIAS and ROUX: Idem. Gaz. méd. de Strasbourg, 10, 1903.

KARCZAG: Über die künstliche Beeinflussung der Allergie bei Tuberkulose. Beitr. z. klin. d. Tuberk., 41, 1919, p. 1.

KIEFER: Statistische und klinische Beiträge zur Lungentuberkulose mit besonderer Berücksichtigung der Kriegseinflüsse. Z. Tbk., 32, 1920. p. 65.

KLING, C.: Untersuchungen über die bakterientötenden Eigenschaften etc. Jena 1910.

KOCH, W.: Die Bluterkrankheit in ihren Varianten. Stuttgart 1889.

KOCH, W.: Der jetzige Stand der Pathologie und Pathogenese der Barlowschen Krankheit und des Skorbuts. D. M. W., 30. Juni 1921, p. 749.

KOHLBRÜGGE: Gärungskrankheiten. C. f. Bakt., Bd. 60, 1911, p. 223.

KORENCHEVSKY, V., and CARR, M.; Biochem. Journ. 17, 1923, p. 187.

KOSSLER: Kl. W., I, 1922, p. 195.

LA MER, VICTOR, and CAMPBELL, H. L.: Changes in organ weight produced by diets deficient in antiscorbutic vitamine. Proc. Soc. Biol. and Med., Vol. 18, No. 1, 1921, p. 32.

LANDAU, M.: Die Nebennierenrinde. Jena 1915.

LANGSTEIN, L.: Welche Aufgaben stellen die Infektionen im Säuglingsalter der Diätetik? Z. f. Kh., 7, 1913, p. 193.

LASÈGUE, CH. and LEGROUX, A.: L'epidémie de scorbut dans la Prison de la Seine et à l'Hôpital de la Pitié. Arch. gén. de Méd., Vol. II, 1871, p. 5; p. 680.

LEICHTENTRITT, B., and ZIELASKOWSKI, M.: Der Gehalt des kindlichen Serums an trypanozider Substanz. Jhrb. Khk., Bd. 98, 1922, p. 310.

LEITNER: W. kl. W., No. 31, 1917.

LESAGE, A.: Maladies du nourrisson. 1911.

LEVEN, M.: Une epidémie de scorbut, observée à l'Hôpital Militaire d' Ivry pendant le siège de Paris 1871. Gaz. méd. de Paris, 1871, p. 430, 469 etc.

LICHTENSTEIN, A.: Pseudoleukämie und Tuberkulose. Virch. Arch., 202, 1910, p. 222.

——: Untersuchungen über die Ätiologie der Lymphogranulomatosis. Frankf. Z. f. Path., Bd. 24, Erg. Hft, 1921, p. 529.

v. LINNÉ, CARL: Collegium diæteticum. 1742. (Printed in: Upsala Universitets Årsskrift, 47: 3, 1907.)

——: De effectu et cura vitiorum diæteticorum. Uppsala 1766.

LOEWY, O.: Scorbut mit Xerose und Hemeralopie. W. med. W., No. 42, 1921, p. 1816.

LOOSER: Jhrb. f. Kh., 62, 1905, p. 743.

LOPEZ-LOMA, M., and RANDOIN, M:me: Production de scorbut chez le cobaye au moyen d'un nouveau régime complet. C. Rend. de l'Acad. de Sc., 176, 1923, p. 1003.

LUBARSCH, O.: Beiträge zur pathol. Anatomie der Unterernährungs- und Erschöpfungskrankheiten. Zieglers Beitr. 69, 1921, p. 242.

——: Handbuch der ärztlichen Erfahrungen im Weltkriege, Bd. 8, 1921, p. 73.

LUST, F., and KLOCMANN, L.: Stoffwechselversuche an Barlow's Krankheit. Jhrb. d. Kh., 75, p. 663.

LÖWENSTEIN: Tuberkuloseimmunität. Kolle-Wassermann's Handb. d. path. Mikoorganismen. Bd. 5, 1913.

MACCALLUM: Textbook of pathology. 1922.

MARTIUS, FR.: Disposition und individuelle Prophylaxe. Brauer-Schröder-Blumenfeld Hb., Bd. 1, 1915, p. 395.

MASSLOW, M.: Zerrüttung des Knochensystems durch phosphorarme Ernährung. Biochem. Z., 64, 1914.

MC CARRISON, R. I.: The pathogenesis of deficiency disease. Journ. Med. Res., Vol. 2, 1919, p. 167.

——: Effect of a scorbutic diet on the adrenalin glands. Brit. Med. Journ., 1919, p. 200.

MCCLENDON, COLE, ENGSTRAND, and MIDDLEKAUFF: The effect of malt and maltextract on scurvy and the alkaline reserve of the blood. Journ. Biol. Chem., 40, 1919, p. 243.

MCCOLLUM, E. V., SIMMONDS, N., and PITZ, W.: The nature of the dietary deficiencies of the wheat embryo. Journ. Biol. Chem., 25, 1916, p. 105.

MEDIN, O.: 15 tilfaelde av Morbus Barlowi. N. mag. f. laegevid., 59, 1898, p. 1016.

——: Om behandlingen af mjölk med vätesuperoxid. Hygiæa, Bd. 70, 1908.

MEYER, AD. H.: Barlows sygdom. København 1901.

MEYER, L. F.: Die Scorbutische Diathese. Mo. f. Khk. 25, 1923, p. 454.

MEYER, L. F., and NASSAU, E.: Über idiopathische Blutungen in Haut etc. Jhrb. Khk., Bd. 94, 1921, p. 341.

MOREL, A., MOURIQUAND, G., MICHEL, P., and THÉVENON, L.: C. Rend. Soc. Biol., Bd. 85, 1921, p. 469.

MOURIQUAND, G.: Scorbut typique avec oedèmes. Lyon Med. 131, 1922, p. 448.

MOURIQUAND, G.. and MICHEL, P.: Adjuvants non antiscorbutiques de la substance antiscorbutique. C. Rend. Soc. Biol. Dec. 1922, p. 1404.

——: Scorbut expérimental. C. Rend. Soc. Biol., Bd. 84, 1921, p. 736.

——: C. Rend. Soc. Biol., Bd. 84, 1921, p. 43; p. 734.

——: De l'action de certains aliments gras sur le métabolism osseux. C. Rend. Soc. Biol., Bd. 86, 1922.

MOURIQUAND, G., MICHEL, P., and BERTOY: Evolution du scorbut expérimental chez le cobaye tuberculisé. Lyon Med. 131, 1922, p. 689.

MOURIQUAND, G., MICHEL, P., and SANYAS, R.: Huile de foie de morue et lésions du type scorbutique. Lyon Med. 132, 1923, p. 360.

MUCH, HANS: Die Immunität. Brauer Schröder-Blumenfeld Hb., Bd. 1, 1915, p. 300.

NAEGELI, O. (senior): Corresp. Bl. f. Schweiz. Ärzte. 1. Okt. 1897.

——, (junior): Zur pathologischen Anatomie und zum Wesen des Morbus Barlow. Z. f. allg. Path. und path. Anat., No. 17, 1897.

NASSAU, E., and SINGER, M. J.: Zur Kentniss des Vorstadiums der Barlowschen Krankheit. Jhrb. f. Khk., Bd. 98, 1922, p. 44.

NOBEL, E.: Zur Barlowfrage. Z. f. Khk., 28, 1921.

ORBAN, B.: Das gegenwärtige Stand der Lehre von den Vitaminen und die Bedeutung der letzteren für das Gebiss. Z. f. Stomat., H. 7, 1923, p. 420.

OSBORNE, T. B., and MENDEL, L. B.: The incidence of phosphatic urinary calculi in rats fed on experimental rations. Journ. Am. Med. Ass., 69, 1917, p. 32.

——: The vitamins in green food. Journ. Biol. Chem., 37, 1919, p. 187; p. 223.

——: Skimmed milk as supplement to corn in feeding. Journ. Biol. Chem., 44, 1920, p. 1.

PARSONS, HELEN: The antiscorbutic content of certain body-tissues of the rat. Journ. Biol. Chem., 44, 1920.

PEIPER, H.: Über den Lipoidgehalt der Nebennierenrinde des Meerschweinchens bei experimentellem Scorbut. Klin. W. I, No. 25, 1922, p. 1263.

PHILIP, R. W.: On raw meat alimentation in tuberculosis. Lancet, 23 Dec. 1905.

——: Tuberculosis of lung. Encycl. Med., Bd. 8, 1922, p. 463.

v. PIRQUET: Die Aufgaben der Küche. Z. f. Kh., 18, 1918, p. 225.

PITZ: Studies of experimental scurvy III. Influence of meats and salts. Journ. Biol. Chem., 36, 1918, p. 439.

POGORSCHELSKY, H.: Zur Frage des Auftretens von Scorbut beim Brustkinde. Z. f. Kh. 35, 1923, p. 244.

PRYM, P.: Allgemeine Atrophie, Ödemkrankheit und Ruhr. Frankf. Z. f. Path., Bd. 22, 1919—20, p. 1.

QUENSEL, U.: Bidrag till kännedomen om den späda barnålderns patologi. Bil. 7 till Allm. Barnhusets årsberättelse år 1898.

RAEBIGER, H.: Das Meerschweinchen. Hannover 1923.

RAISONNIER: La Zomothérapie. Thése de Paris. 1902.

RENON: Bull. gén. de thér., 168, 30 Juillet 1914, p. 91.

RHEINDORF by TÜCHLER: Über Scorbut. Med. Klin., No. 5, 1918.

ROBB, E. F., MEDES, GRACE, MCCLENDON, J. F., GRAHAM, MARG., and MURPHY, I. J.: A study of scurvy and its bearing on the preservation of the teeth. Journ. Dent. Res., March 1921, p. 39.

RÖMER, P., and JOSEPH, K.: Experimentelles Tuberkulosestudium. Zieglers Beitr. klin. Tub., 17, 1910.

RONDONI, P., and MONTAGNANI, M., quoted after FUNK.

ROSENBUND. F.: Allgemeinschädigungen im Rahmen des Säuglingsscorbuts. Z. f. Khk., Bd. 34, 1923, p. 333.

SALLE, V., und ROSENBERG, M.: Über Scorbut. Erg. d. inn. Med. u. Khk., Bd. 19, 1921, p. 31.

SATO, T., und NAMBU, K.: Zur Pathologie und Anatomie des Scorbuts. Virch. Arch., Bd. 194, p. 151.

SAXL, R., und MELKA, J.: Über den Scorbut. Med. Klin., No. 37, 1918, p. 886.

SCHMORL, G.: Über die Pathogenese der bei Möller-Barlowscher Krankheit auftretenden Knochenveränderungen. Jhrb. f. Khk., 35, 1902.

——: Die pathologische Anatomie der rachitischen Knochenerkrankung. Erg. d. inn. Med. u. Khk., Bd. 4, 1909, p. 403.

——: Zur pathologischen Anatomie der Barlowschen Krankheit. Zieglers Beiträge z. path. Anat. 30, 1901, p. 215.

SCHOEDEL, J., and NAUWERCK, C.: Untersuchungen über die Möller-Barlowsche Krankheit. Jena 1900.

SCHULZ, A.: Über die Chromotrophie des Gefässbindegewebes. Virch. Arch. Bd. 239, H. 3.

SELTER, H., and NEHRING: Einfluss der Ernährung auf die Tuberkulosesterblichkeit. Z. f. Tuberk., Bd. 34, 1921, p. 1.
SHERMAN, H. C., LA MER, V. K., and CAMPBELL, H. L.: Quantitative determination of the antiscorbutic vitamin. Journ. Am. Chem. Soc., 44, 1922, p. 165.
SHERMAN, H. C., and SMITH: The vitamins. Am. Chem. Soc. Mon. Ser., New York 1922.
SMITH, M.: Am. Rev. of tuberculosis. 7, 1923, p. 33.
STEINITZ, F.: Über den Einfluss von Ernährungsstörungen auf die chemische Zusammensetzung des Säuglingskörpers. Jhrb. f. Khk. 59, 1904, p. 446.
STEINITZ, F., and WEIGERT: Über Demineralisation und Fleischtherapie bei Tuberkulose. Jhrb. f. Khk., 61, 1905.
STILL, G. F.; Brit. Med. Journ., July 31, 1920, p. 156.
STOELTZNER, W.: Zur diätetischen Behandlung der Tuberkulose. B. kl. W., 1920, p. 981.
THOMAS, E.: Biochem. Z., 57, 1913, p. 456.
THOMAS, E.: Über die Beziehung chronischer Unterernährung zur Infektion. Z. Kh., 11, 1914, p. 317.
TOBLER, W.: Der Scorbut im Kindesalter. Z. f. Kh., Bd. 18, Orig., 1918, p. 63.
TOVERUD, G.: Caries dentis. Norsk tandlaegefor. tid., Dec. 1923.
——: Journ. Am. Dent. Ass., No. 3, 1923, p. 207.
TOZER, F. M.: The effect on the guinea-pig of deprivation of vitamin A. Journ. Path. and Bact., Bd. 24, 1921, p. 306.
UMBER: Med. Klin., Bd. 18, 1922, p. 851.
VOGT: Säuglingsscorbut. Jhrb. f. Kh. 91, 1920, p. 278.
WALLGREN, A.: Acta Pædiatrica. Vol. II, 1923, pp. 376.
——: Wahl der Versuchstiere für experimentelle Tuberkulosestudien. Brauers Beitr. z. Klinik d. Tuberk., Bd. 47, 1921, s. 425.
——: Zur Symptomatologie und Pathogenese der oedema scorbuticum invisibile. Z. f. Khk., 1922, p. 35.
WEIL, E., and MOURIQUAND, G.: Journ. physiol. path., 17, 1918, p. 849.
WEINERT, A.: Über phtisische Infectionen. Hdb. d. ärztl. Erfahr. im Weltkriege., Bd. 8.
WIELAND: Bruning & Schwalbe, Hdb. d. allg. Path. d. Kindesalters. 2: 1, 1913, p. 281.
WIENBERGER: Möller-Barlowsche Erkrankung. Klin. Wochenschr., I, No. 4, 1922, p. 119.
ZILVA, S. S.: Influence of deficient nutrition on the production of agglutinin etc. Biochem. Jl. 13, 1919, p. 172.
——: Influence of aëration etc. Lancet 1921, I, p. 478.
——: Conditions of inactivation etc. Biochem. Jl. 16, 1922, p. 42.

ZILVA, S. S., and WELLS, F. M.: Changes in the teeth etc. Proc. Roy. Soc. London. B. 90, p. 505.

The old literature, not mentioned here, may be found in the books of W. KOCH (1889) and AD. MEYER (1901).

List of authors.

A.

Abderhalden 83, 134, 153, 265.
Abels 118, 119, 265.
Adams 145, 265.
Andersson 12, 265.
Aron 32, 125, 265.
Aschoff 51, 53, 54, 55, 56, 57, 58, 59, 66, 67, 70, 71, 76, 77, 79, 80, 82, 83, 91, 92, 96, 100, 110, 111, 113, 116, 132, 144, 265.

B.

Baginsky 49, 265.
Bardin 265.
Bahrdt 65, 127, 265.
Barlow 49, 69, 111, 119, 142, 265.
Barnes 25, 265.
Bartenstein 138, 265.
Baumann 83, 265.
Baumgarten 157.
Bedson 108, 109, 110, 265.
Bergheim 13, 268.
Bertoy 147, 272.
Beitzke 144, 265.
Berg 132, 265.
Bezssonoff 14, 265.
Bierich 100, 109, 116, 123, 136, 147, 266.
Bolle 138, 266.
Brandt 108, 266.
Broderich 132.

C.

Campbell 11, 130, 270, 274.
Carr 12, 270.
Carrell 115, 266.
Chick 9, 11, 13, 17, 25, 123, 124, 139, 266.
Cohen 9, 16, 129, 266.
Cole 15, 271.
Cordier 125, 266.
Cornet 140, 266.
Coward 27.
Cramer 92, 136, 266.

D.

Dahle 12, 266.
Dalyell 124, 139, 266.
Darling 137, 266.
Davey 26, 266.
Delf 12, 13, 27, 33, 36, 66, 266.
Drummond 9, 266.
Dutcher 12, 25, 265, 266.

E.

Eckles 12, 265, 266.
Edelstein 65, 127, 265.
Ellis 12, 267, 268.
Emhoff 151, 270.
Engstrand 15, 271.
Epstein 100, 124, 267.
Erdheim 79, 267.

F.

Faber 13, 267.
Findlay 80, 101, 109, 112, 113, 267.
Finkelstein 24, 25, 26, 117, 122, 124, 267.
Fortenato 121.
Fraenkel 48, 49, 50, 55, 56, 60, 65, 109, 111, 112, 126, 129, 130, 267.
Frank, H., 124, 267.
Frank, M., 60, 127, 267.
Freise 267.
Freudenberg 134, 267.
Frölich 9, 10, 12, 13, 16, 25, 29, 57, 59, 64, 69, 71, 76, 116, 117, 129, 131, 138, 267, 269.
Funk 9, 27, 99, 267.
Fürst 22, 267.

G.

Geoghegan 146, 267.
Gerhartz 143, 148, 156, 267.
Gerstenberger 127, 267.
Givens 13, 267.
Godlevski 33, 268.

Gougerot 158.
Graham 17, 39, 46, 49, 129, 273.
Grüner 151, 268.
György 134, 176, 268.

H.

Hall 25, 266.
Hamburger 151, 268.
Hamilton 145, 265.
Happ 147, 268.
Harden 268.
Hart, C., 9, 30, 48, 49, 50, 53, 57, 58, 69, 76, 78, 79, 80, 83, 100, 109, 110, 111, 124, 136, 147, 266, 268.
Hart, E., 3, 12, 25, 268.
Hausmann 83, 109, 268.
Hawk 13, 268.
Hayem 69, 76, 79, 82, 96, 268.
Héricourt 141, 268.
Hershaw 25, 266.
Herxheimer 77, 268.
Herzog 54, 71, 109, 126, 268.
Hess 9, 11, 13, 16, 17, 18, 25, 26, 29, 30, 33, 39, 54, 64, 65, 68, 70, 89, 91, 92, 96, 108, 109, 110, 116, 120, 122, 124, 125, 126, 128, 132, 133, 136, 137, 146, 163, 268.
Heubner 124, 269.
Hirschsprung 91.
Hoffman 129, 269.
Holmgren 77, 269.
Holst 9, 10, 12, 13, 14, 16, 25, 26, 29, 30, 57, 59, 64, 69, 71, 76, 116, 117, 129, 131, 138, 269.
Horne 13, 265.
Hopkins 9, 12, 13, 269.
Howard 83, 128, 265, 269.
Howe 17, 36, 40, 46, 49, 126.
Hume 9, 11, 13, 25, 123, 266.
Häggquist 47.
Höjer 158, 160, 269.

I.

Ide 113, 269.
Ingier 53, 55, 57, 70, 100, 110, 111, 112, 147, 269.
Ingvaldsen 128, 269.
Iwabuchi 54, 55, 57, 83, 101, 103, 109, 110, 128, 137, 269, 270.

J.

Jackson 39, 69, 112, 117, 270.
Jacobsthal 51, 53, 69, 100, 111, 270.
Jansen 137, 270.
Joest 151, 270.
Joseph 159, 273.
Josias 141, 270.

K.

Kaiserling 145.
Karczag 142, 270.
Kassowitz 147.
Kiefer 143, 270.
Kirch 108.
Kling 158, 270.
Klocmann 96, 127, 128, 271.
Koch, W., 51, 53, 54, 55, 56, 57, 58, 59, 66, 67, 70, 71, 76, 77, 79, 80, 82, 83, 91, 92, 96, 100, 110, 111, 112, 116, 132, 144, 265, 270.
Koch, W., 33, 79, 82, 109, 111, 112, 119, 124, 270.
Kohlbrügge 270.
Korenchevsky 12, 270.
Kossel 140, 266.
Kossler 125, 270.

L.

La Mer 11, 130, 270, 273.
Landau 101, 270.
Langstein 270.
Lasègue 69, 270.
Legroux 69, 270.
Leichtentritt 116, 119, 121, 270.
Leitner 109, 270.
Lesage 33, 270.
Lessing 9, 30, 38, 48, 49, 50, 53, 57, 58, 69, 76, 78, 79, 80, 83, 100, 109, 110, 111, 124, 136, 147, 268.
Leven 69, 79, 82, 271.
Lichtenstein 158, 160, 271.
v. Linné 82, 136, 140, 271.
Loeb 136.
Loewy 138, 271.
Looser 70, 111, 112, 119, 271.
Lopez Loma 11, 13, 271.
Lubarsch 133, 137, 271.
Lukin 82, 91.
Lust 96, 127. 128, 271.
Löwenstein 140, 271.

M.

Mac Callum 8, 66, 271.
Martinotti 103, 271.
Martius 141, 271.
Masslow 14, 271.
McCarrison 89, 100, 101, 104, 110, 125, 133, 137, 271.

McClendon 15, 17, 39, 46, 49, 271, 273.
McCluggage 13, 267, 268.
McCollum 11, 33, 123, 271.
Mead 12, 266.
Medes 17, 39, 46, 49, 129, 273.
Medin 12, 61, 63, 271.
Melka 113, 273.
Mellanby 113, 132.
Mendel 9, 16, 99, 129, 266, 272.
Mengering 136.
Meyer, Ad., 79, 271, 274.
Meyer, L. F., 124, 272.
Michel 13, 14, 128, 129, 130, 147, 162, 272.
Middlekauff 15, 271.
Monrad 12.
Montagnani 100, 101, 273.
Moore 39, 69, 112, 117, 270.
Morel 128, 272.
Mottram 92, 136, 266.
Mouriquand 13, 14, 128, 129, 130, 147, 162, 272, 274.
Much 141, 272.
Murphy 17, 39, 46, 49, 129, 273.

N.

Naegeli 109, 147, 272.
Nambu 69, 79, 80, 82, 91, 273.
Nassau 119, 272.
Nauwerk 10, 100, 273.
Nehring 144, 273.
Nobel 137, 138, 140, 272.
Noeggerath 137.

O.

Orban 132, 272.
Osborne 99, 272.

P.

Padua 99.
Parsons 23, 89, 272.
Peiper 13, 101, 273.
Philip 141, 273.
v. Pirquet 138, 139, 273.
Pitz 11, 123, 128, 271, 273.
Prym 137, 273.

Q.

Quensel 61, 62, 63, 130, 273.

R.

Raebiger 15, 273.
Raissonnier 141, 273.
Randoin 11, 13, 271.
Reinert 91.
Renon 273.
Rheindorf 108, 113, 273.
Richet 141, 268.
Robb 17, 39, 46, 49, 128, 273.
Rondoni 100, 101, 273.
Rosenberg 109, 110, 116, 136, 146, 163, 273.
Rosenbund 14, 273.
Roux 141, 270.
Römer 159, 273.

S.

Salle 109, 110, 116, 136, 146, 163, 273.
Sato 69, 79, 82, 91, 273.
Saxl 113, 273.
Schmorl 49, 50, 66, 111, 112, 147, 273.
Schoedel 10, 49, 51, 52, 55, 56, 57, 63, 69, 100, 111, 124, 130, 147, 273.
Schulz 32, 80, 107, 108, 273.
Selter 144, 274.
Shaefer 12, 266.
Sherman 11, 13, 16, 17, 130, 131, 274.
Simmonds 11, 271.
Singer 119, 272.
Skelton 9, 266.
Smith 16, 147, 149, 268, 274.
Sonnenburg 56.
Steinitz 137, 141, 274.
Stéenbock 12, 27, 266, 268.
Sternberg 158.
Still 27, 274.
Stoeltzner 143, 274.
Stoerk 158.
Supplee 25, 269.
Swiderski 111, 112.

T.

Tailor 132.
Thévenon, L, 128, 272.
Thomas 142, 274.
Tobler 24, 108, 109, 274.
Toverud 40, 45, 46, 49, 65, 104, 106, 107, 109, 126, 274.
Tozer 12, 13, 33, 36, 66, 266, 274.

U.

Umber 24, 108, 109, 110, 274.
Unger 13, 25, 268, 269.
Urizio 82.

V.

Variot 82.
Virchow 135.
Vogt 116, 274.

W.

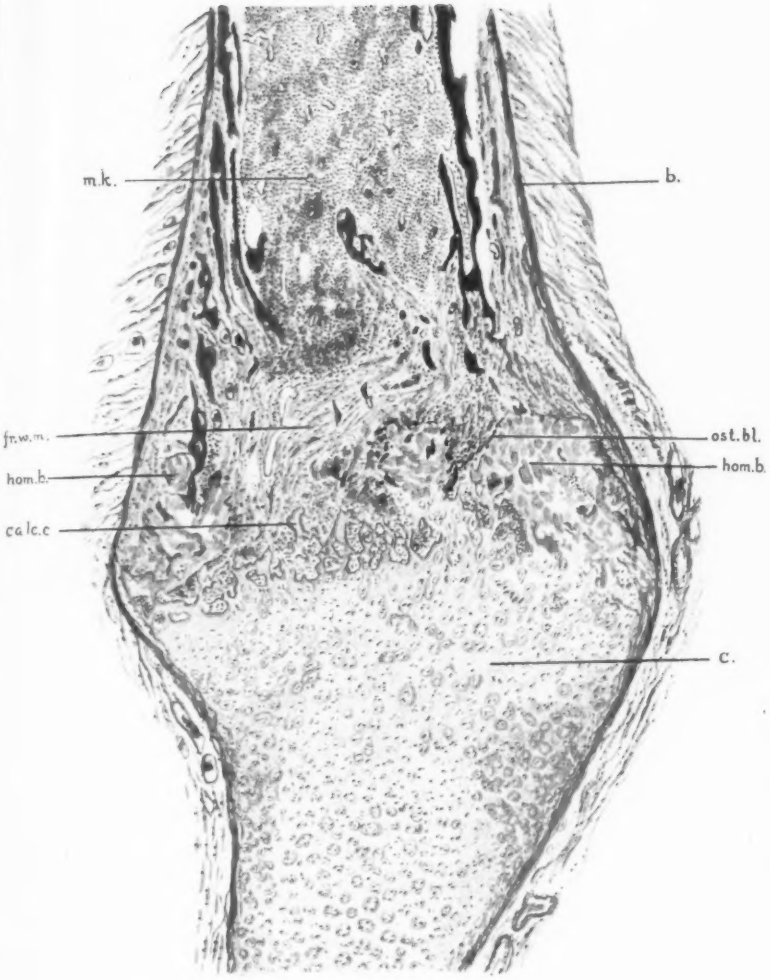
Wagner 82, 147, 268.
Wallgren 116, 137, 148, 150, 274.
Wassermann 108.
Weigert 141, 142, 144, 274.
Weil 274.
Weinert 144, 274.
Wells 39, 45, 46, 147, 274.
Wertheimer 83, 134, 265.
Wieland 14, 122, 274.
Wienberger 58, 274.
Wilbur 12, 265.

Z.

Zielaskowsky 116, 119, 121, 270.
Zilva 12, 13, 39, 45, 46, 121, 268, 274, 275.

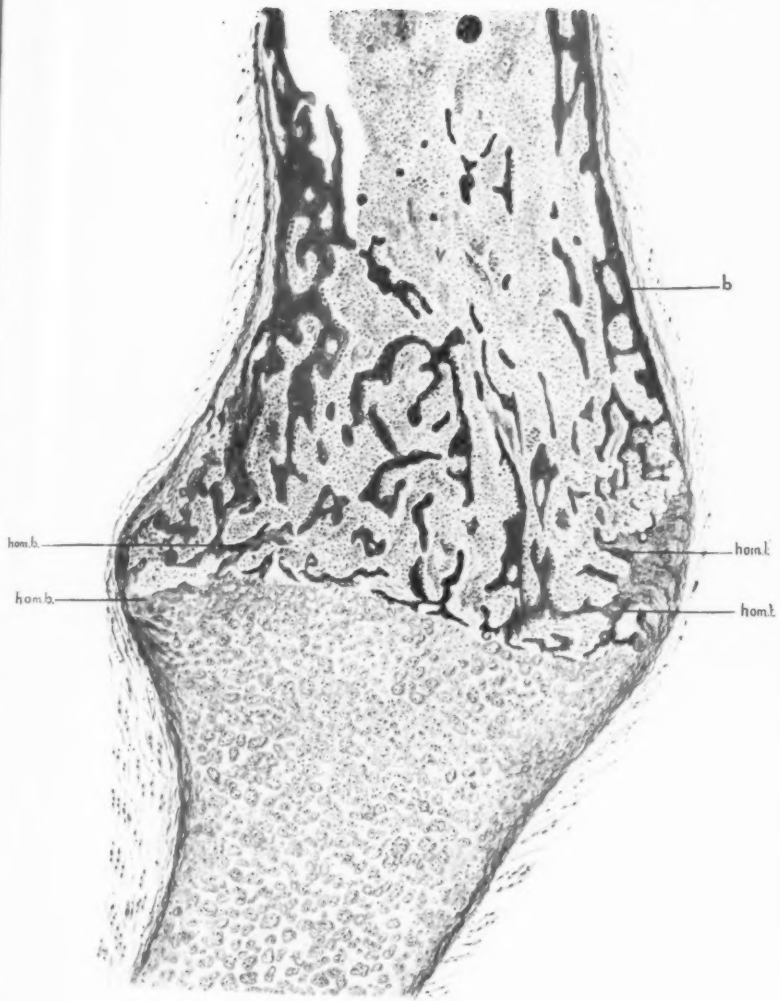
Erratum.

P. 141, l. 6, *for* Madsen *read* Martius.



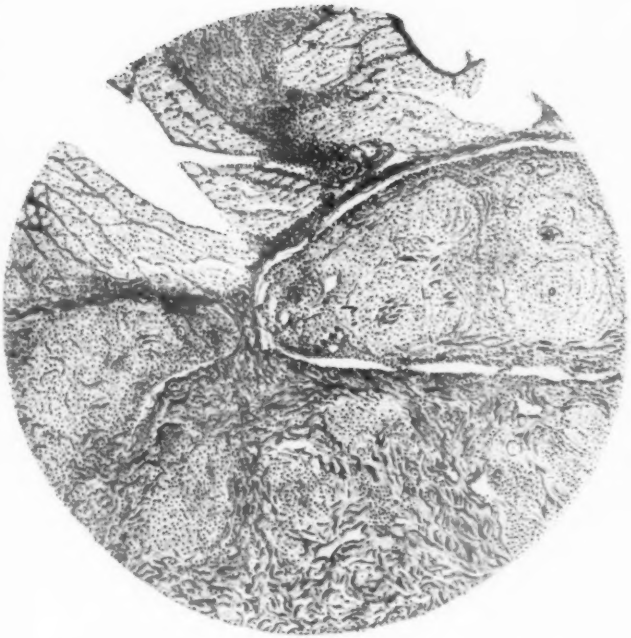
Scorbut manifestus mitior. No. 75.

Frontal section of rib, × 28.
Connective tissue staining of Hansen.
Atrophy of the collagen substance in cartilage *(c)* and bone *(b)*.
No collagen in the new scorbutic bone *(hom. b.)*.
***m. k.* megakaryocyts. *fr. w. m.* frame-work marrow.**

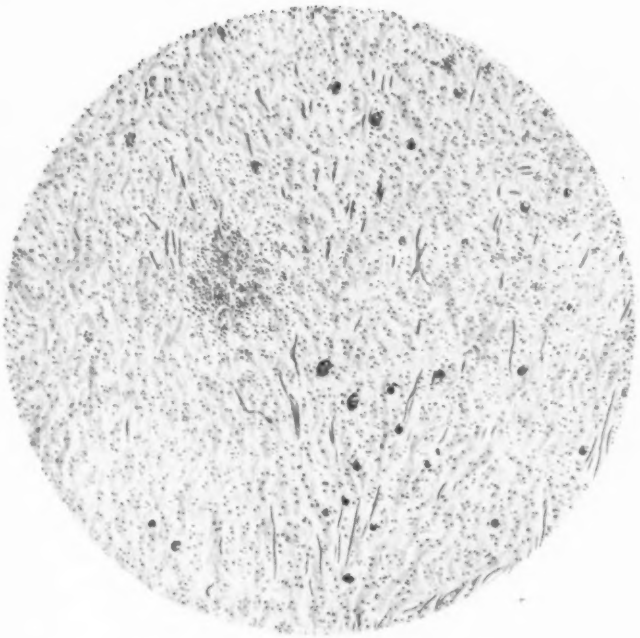


Healing scurvy. No. 76.

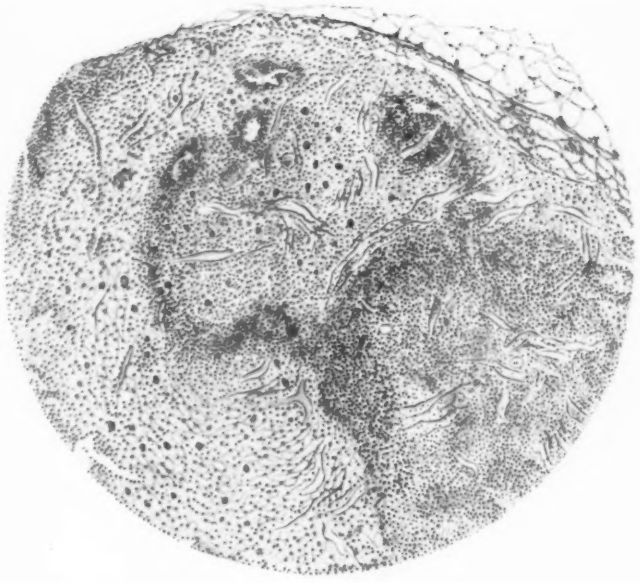
Frontal section of rib, × 28.
Connective tissue staining of Hansen.
Reorganisation of the costochondral junction.
Remaining beams of collagen-free bone *(hom. b.)* enclosed in the system of more normal bone-columns *(b)*.



No scurvy. Complete dietary. No. 108. 102 days.
Tuberculous focus in muscle. Necroses penetrated and surrounded by connective tissue with strong collagen fibrils.

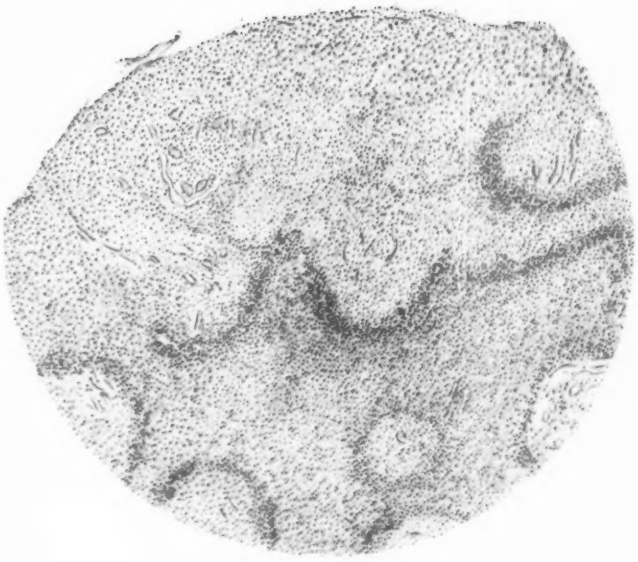


Scorbut mitior manifestus, 0,1 m. pr. d. 24 days. No. 124.
Tuberculous focus in muscle. Necrosis. Inconsiderable collagen substance.



No scurvy. Complete dietary. No. 172. 24 days.

Tuberculous necroses in regional lymph gland, penetrated and surrounded by connective tissue with strong collagen fibrils.



Scorbut mitior manifestus, 0,1 m. pr. b. 43 days.
Tuberculous necroses in regional lymphglands. Inconsiderable collagen substance.

Acta Chirurgica Scandinavica

Editor: **Einar Key,** *M. D., Riddaregatan 1, Stockholm, Sweden*
Editorial Staff: in Denmark P. N. Hansen, V. Schaldemose; *in Finland* R. Faltin, A. Krogius; *in Norway* P. Bull, J. Nicolaysen; *in Sweden* E. Key, G. Petrén.
Subscription: 20 Sw. crowns

Acta Dermato-Venereologica

Editor: **Johan Almkvist,** *M.D., Hospital St. Göran, Stockh., Sweden*
Editorial Staff: in Holland S. Mendes Da Costa; *in Normay* E. Bruusgaard; *in Sweden* J. Almkvist; in *Czecho-Slovakia* F. Šamberger.
Subscription: 20 Sw. crowns, or $ 5, or 25 s., or 40 Fr. francs or 50 It L.

Acta Gynecologica Scandinavica

Editor: **Hj. Forssner,** *M.D., Klara Norra Kyrkog. 26, Stockholm, Sweden*
Editorial Staff: in Denmark S. A. Gammeltoft; *in Finland* W. Wegelius; *in Norway* Kr. Brandt; *in Sweden* Hj. Forssner.
Subscription: 25 Sw. crowns

Acta Medica Scandinavica

Editor: **I. Holmgren,** *M. D., Seraphimer Hospital, Stockholm, Sweden*
Editorial Staff: in Denmark H. I. Bing, K. Faber; *in Finland* R. Ehrström, T. W. Tallqvist; *in Norway* P. F. Holst, S. B. Laache; *in Sweden* I. Holmgren, K. Petrén.
Subscription: 20 Sw. crowns, or $ 5,50, or 25 s., or 40 Fr. francs

Acta Oto-Laryngologica

Editor: **Gunnar Holmgren,** *M.D., Hospital Sabbatsberg, Stockholm, Sweden*
Editorial Staff: in Denmark E. Schmiegelow; *in Finland* A. af Forselles; *in Holland* H. Burger; *in Norway* V. Uchermann; *in Sweden* R. Bárány, G. Holmgren.
Subscription: 25 Sw. crowns

Acta Paediatrica

Editor: **I. Jundell,** *M. D., Artillerigatan 3, Stockholm, Sweden*
Editorial Staff: in Denmark C. E. Bloch, S. Monrad; *in Finland* Elis Lövegren, Arvo Ylppö; *in Holland* E. Gorter, J. Haverschmidt, Cornelia de Lange; *in Norway* Th. Frölich, Axel Johannessen, Carl Looft; *in Sweden* I. Jundell, A. Lichtenstein, Wilh. Wernstedt.
Subscription: 20 Sw. crowns, or 25 s., or $ 5 or 40 Fr. francs or 50 It. L.

Acta Radiologica

Editor: **Gösta Forssell,** *M. D., Bergsgatan 2, Stockholm, Sweden*
Editorial Staff: in Denmark H. J. Panner, A. Reyn; *in Finland* G. A. Wetterstrand; *in Holland:* L. G. Heilbron, N. Voorhoeve; *in Norway* S. A. Heyerdahl, H. Thue; *in Sweden* L. Edling, G. Forssell.
Subscription: 25 Sw. crowns, or $ 6, or 32 s. or 70 Fr. francs

---

The articles in the Acta are published in English, French or German according to the decision of the author. Each volume comprises 500—600 pages, distributed in 4—6 occasional numbers

Subscriptions, manuscripts and advertisements for the Acta should be forwarded under the names of the respective Acta, adress: STOCKHOLM, SWEDEN.

INDEX ACTORUM.

Pag.

J. Axel Höjer: Studies in Scurvy 1